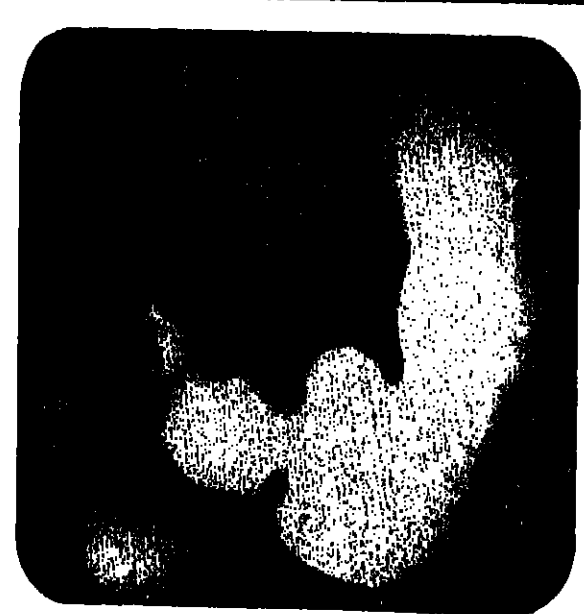


The Pseudo-ulcer



Ulcer-like symptoms: no G.I. pathology

The patient is convinced it's an ulcer. However, symptoms are not quite typical, and x-ray findings are negative. These findings and the results of additional diagnostic procedures exclude an organic basis for the patient's complaints. A diagnosis of "upper functional gastrointestinal disorder" is made, which is supported by the fact that episodes of painful symptoms coincide with episodes of excessive anxiety, as indicated by the history.

It may be useful to explain to the patient the mechanism by which emotions upset normal G.I. functioning, resulting in hypersecretion and hypermotility and thus causing such symptoms as nausea and epigastric pain. In upper functional gastrointestinal disorders, counseling by the primary physician can often help the patient to understand how excessive anxiety may cause flare-ups of G.I. symptoms.

A disproportionate number of patients seen by the general practitioner suffer from functional disorders, as do more than half of those seen by the gastroenterologist.* Where milder cases may respond to counsel-

ing alone, if symptoms are severe and disabling to any degree, a suitable regimen may include medication to reduce the symptoms and the excessive anxiety that often provokes these distressing symptoms.

In these cases, Librax as an adjunct can greatly contribute to the course of therapy. Its dual action can offer relief of both painful symptoms and excessive anxiety, because each capsule contains 5 mg chlorthalidone HCl and 2.5 mg clidinium Br. The antianxiety action of Librium® (chlorthalidone HCl) makes Librax exceptional

An adjunct in anxiety-related upper functional G.I. disorders

Librax®

Each capsule contains 5 mg chlorthalidone HCl and 2.5 mg clidinium Br.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Symptomatic relief of hypersecretion, hypermotility and anxiety and tension states associated with organic or functional gastrointestinal disorders; and as adjunctive therapy in the management of peptic ulcer, gastritis, duodenitis, irritable bowel syndrome, spastic colitis, and mild ulcerative colitis.

Contraindications: Patients with glaucoma; prostatic hypertrophy and benign bladder neck obstruction; known hypersensitivity to chlorthalidone hydrochloride and/or clidinium bromide.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering Librium (chlorthalidone hydrochloride) to known addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions) following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in

pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards. As with all anticholinergic drugs, an inhibiting effect on lactation may occur.

Precautions: In elderly and debilitated, limit dosage to smallest effective amount to preclude development of ataxia, overmedication or confusion (not more than two capsules per day initially; increase gradually as needed and tolerated). Though generally not recommended, if combined therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients. Employ usual precautions in treatment of psychiatric states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: No side effects or manifestations not seen with either compound alone have been reported with Librax. When chlorthalidone hydrochloride is used alone, drowsi-

ness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, tinnitus, menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally with chlorthalidone hydrochloride, making periodic blood counts and liver function tests advisable during protracted therapy. Adverse effects reported with Librax are typical of anticholinergic agents, i.e., dryness of mouth, blurring of vision, urinary hesitancy and constipation. Constipation has occurred more often when Librax therapy is combined with other antispasmodics and/or low residue diets.

*Rome HP, Brannick TL: Orientation and mechanism of functional disorders; clinicalphysiologic correlation, chap. 135, in *Gastroenterology*, edited by Bockus HL, Philadelphia, WB Saunders Company, 1965, p. 1116



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Medical Tribune

Vol. 16, No. 16

world news of medicine and its practice—fast, accurate, complete

and Medical News
Wednesday, April 23, 1975

making rounds

at press time

MALPRACTICE-IDAHO: Legislation limiting liability to \$150,000 for injury to one person will take effect June 1, legislature acting overwhelmingly after Argonaut Co. announced termination of coverage to M.D.s and 300% premium hike for hospitals. New law also limits attorney's fees, permits hospitals and M.D.s to form own insurance firms, authorizes emergency creation of joint underwriting association composed of all casualty companies in state. Sources at state medical association told *MT* there have been few big suits and awards, but premiums have reflected situation in other states.

MALPRACTICE-MD: In Maryland, laws imposing \$300 tax on M.D.s to capitalize new insurance co., and requiring all carriers in state to share in writing malpractice coverage, were enacted by Assembly. May 31 is date announced by St. Paul Fire and Marine for quitting state. Assembly also approved reduction of liability from 8 to 5 years. Bill seeking to take malpractice cases out of courts is not expected to pass.

OPERATING ROOMS in Chicago are in use only 53 per cent of the time that they are staffed and ready, says a Chicago Hospital Council study. Optimum utilization is 75-80 per cent. Biggest cause of underutilization is preference of surgeons to operate mornings. Authors of study suggest new system of "block" scheduling whereby hours would be assigned and reserved, and incorporation of little-used "specialty rooms" into larger operating theaters. Early response of administrators and surgeons has been encouraging; Howard F. Cook, president of Council, told *MT*, adding, "I wouldn't be surprised if this problem is nation-wide."

Cytomegalovirus Infections At Birth Linked to Low IQs

By FRANCES GOODNIGHT
Medical Tribune Staff

NEW YORK—Follow-up studies of young children who had at birth excreted cytomegalovirus (CMV) have shown that such congenital infection is associated with lower IQs than the levels found among matched or random controls, and may also be "a significant cause" of profound deafness.

These findings emerged from detailed examinations of 44 children tested 3.5 to seven years after their birth, Dr. James B. Hanshaw, of the University of Rochester School of Medicine and Dentistry, reported here.

The study population included all but nine of the 53 infants discovered to have cord sera positive for CMV-IgM antibody when 8,644 consecutive sera specimens were tested at a Rochester hospital between 1967 and 1970. One positive infant had lived only a short time, another was stillborn, and the remaining seven positives were unavailable for examination.

Most children with congenital CMV infection are asymptomatic in the newborn period and fewer than 5 per cent exhibit clinical signs that arouse suspicion of CMV infection, Dr. Hanshaw emphasized at a symposium presented by the New York University School of

Continued on page 13



A patient with congenital cytomegalovirus infection detected by screening of cord serum for CMV-IgM antibody. The patient is microcephalic, hypotonic, and deaf, and has psychomotor retardation. No abnormalities were noted during the newborn period, according to Dr. James Hanshaw.

Complications No Matter CPK Isoenzyme Sensitive Index Of Infarct's Size

Medical Tribune Report

HOUSTON—The size of a myocardial infarct can be evaluated accurately even in patients with complicated infarction by analyzing serum values of one isoenzyme of creatine phosphokinase (CPK), the American College of Cardiology was told here.

Investigators at Washington University School of Medicine said that this "MB" isoenzyme is found primarily in myocardium and thus provides a "sensitive and more specific index of myocardial damage than total CPK," which reflects release of enzyme from non-cardiac sources.

They noted that noncardiac CPK may influence serum activity after intramuscular injection, hypotension, or shock.

In a separate report, members of the research group also presented evidence that assays of the MB isoenzyme in serum samples from patients undergoing cardiac catheterization can distinguish the CPK elevations accompanying these procedures from CPK elevations associated with myocardial infarction.

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MD Resistance to PSROs Dying—Simmons

By EDWARD GROSSMAN
Medical Tribune Staff

NEW YORK—If the network of Professional Standards Review Organizations, plans for which must be submitted in 203 districts nationwide by Jan. 1, 1976 runs into trouble, it won't be because of resistance or non-cooperation on the part of physicians, according to Dr. Henry E. Simmons, Deputy Assistant Secretary of Health.



DR. SIMMONS

It will be on account of budgetary cuts plaguing many government projects.

Despite the cuts, the Office of Professional Standards Review of H.E.W. will soon announce a new funding cycle that will expand the program and allow 50 to 60 new districts to join the more than 90 in which compliance plans submitted by physicians have been approved and awarded contracts, and 13 in which PSRO is actually in operation. This guardedly optimistic forecast

for PSROs was made by Dr. Simmons during an interview with *MEDICAL TRIBUNE*.

"Resistance is rapidly dying out among physicians, and no wonder," Dr. Simmons said. "By and large they realize that PSRO is their best, and maybe last, chance to have a hand in improv-

ing health care without compromising their professional standing and responsibility.

"The proof of this is that increasing numbers of districts are giving us their plans, and many state medical societies that had previously been opposed have

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Survey Finds Little Change In Clinician Use of Rauwolfia

By HARRIET PAGE
Medical Tribune Staff

NEW YORK—Clinicians appear not to have made any substantial changes in their use of rauwolfia derivatives, such as reserpine, in the wake of conflicting studies concerning links between these drugs and cancer, *MEDICAL TRIBUNE* found in telephone interviews.

These studies have, in the past six months, claimed an association between rauwolfia derivatives and breast cancer, shown no association between the use of rauwolfia and cancer, and left hanging the possibility of a connection between hypertension and cancer.

Dr. Rita Kelly, a medical oncologist at Massachusetts General Hospital, summed up the situation as "muddy." She has not seen any relationship between rauwolfia compounds and cancer in her patients and, she said, "I have not stopped reserpine in women who have had breast cancer and have been on the drug for a long time, and who are under good control with the reserpine, because hypertension is a bad disease, too."

She is inclined to view the retrospective studies in general as "not terribly helpful," she said. "The correlation is

Continued on page 14

Ind. MDs Look to Panel Plan To Relieve Malpractice Bind

By MICHAEL HERRING
Medical Tribune Staff

INDIANAPOLIS—Indiana physicians, facing the uncertain future of choosing between malpractice insurance premiums of \$18,000 to \$25,000 a year, or none at all, are working with the state legislature to enact measures that will hopefully eliminate unfairness in malpractice litigation.

A bill calling for the formation of pretrial screening panels—special teams of three doctors who will review malpractice suits and present their findings to a court of law—is before the state Senate, according to Dr. Paul F. Müller, co-chairman (with Dr. Bill Cast) of the State Medical Association committee supporting the bill's passage.

Makeup of Panel

The panels would consist of one doctor chosen by the plaintiff, one by the defendant, and a third by the first two panelists, Dr. Müller told MEDICAL TRIBUNE. In cases of dispute over panelists, the court may appoint all three.

"The panelists are subject to subpoena as witnesses in the jury trial, and their decision is admissible as evidence in court by either party in the suit," he added.

Under the bill, only the first \$100,000 of any award is paid by the physician's insurance, thus setting a cap on insurer losses, Dr. Müller explained. A patient may win up to \$400,000 more, he said, but this portion of any judgment will be paid from a special "catastrophic fund," with money provided by a 10 per cent surcharge on all malpractice insurance policies in the state.

The bill passed by the House originally called for a full-time Patient's Compensation Board—two physicians, two attorneys, and two lay people who would hear and decide all malpractice cases in the state. The members were to be nominated by state bar and medical associations and appointed by the Governor. This bill was to guarantee full payment to the patient of any award up to \$100,000, make attorney fees independent of plaintiff award, set a cap on insurance payments, and prevent subrogation by the patient's health insurer. Expert witnesses were built into this plan and an additional \$100,000 maximum award for catastrophic cases would be paid from a fund maintained by the local medical community, Dr. Müller told MEDICAL TRIBUNE.

Elimination of Nuisance Cases

"The big value of the panel is the elimination from the courts of nuisance cases," Dr. Müller said. As soon as the panel labels a case 'nuisance,' the plaintiff's attorney will give it up, knowing this will be introduced as evidence.

"In the past attorneys have submitted cases without merit because they know the insurance companies won't fight them and will settle out of court for some minimal payment. This has driven up insurance rates and slowed down the whole legal process."

"I think very few cases will go to court under the new bill. If a case is meritorious, both attorneys now know

there's a limit to what they can win or lose in court, so I think they'll settle beforehand. Either way, a case may now be decided in two to four months, rather than years," he said.

Dr. Müller, who is Medical Director of St. Vincent's Hospital here, also outlined other features of the bill:

- Liability of two years for adults, and two years after the age of six for children. After this, the doctor is no longer responsible for the patient's well-being.
- No more "ad damnum" or "breach of warranty" suits. The former (loosely translated, "the prayer") is the "half-a-million-dollar suit that hits the headlines and makes the doctor look horrible," Dr. Müller explained. Now the patient may sue only for damages, not a sum of money, and this will not receive much public notice, he said.

A "breach of warranty" suit occurs when a doctor has tried to assure a patient in distress by saying, "Don't worry, we'll take care of you." Then he is sued on the grounds that he guaranteed that the patient's disease could be cured, Dr. Müller said. "Now they can't sue for that unless the doctor puts this in writing and no doctor would dare do that."

While he believes that "there's no opposition to the bill at this point," and expects it to become law this week, Dr. Müller concluded, "It's not law yet—and there's many a slip between the cup and the lip."

Egeberg Applauds Effort

Dr. Roger O. Egeberg, Special Assistant to H.E.W. Secretary for health policy and assigned to the national problem of physician insurance, attended hearings for the Indiana bill.

"I was amazed at how far they've gotten in Indiana," he told MEDICAL TRIBUNE. "Their interest and sense of responsibility in taking hold of the issue on a local level is the key to the overall problem. It should be handled by individual states, unless there is a breakdown in getting insurance. Then

From Alcoholism to Pancreatitis Via Triglyceridemia?

By RALPH COSHAM
Special Tribune Correspondent

TUCSON, ARIZ. — Increased serum triglycerides may play an important role in the pathogenesis of acute pancreatitis in some alcoholics, Dr. John L. Cameron told the annual meeting of the Society of University Surgeons here.

Dr. Cameron, of the Department of Surgery, Johns Hopkins Hospital, Baltimore, Md., said that although excessive consumption of alcohol is known to cause episodes of acute pancreatitis, the mechanism is unknown.

"The most widely accepted theory is that alcohol ingestion causes partial pancreatic duct obstruction and an increase in pancreatic secretory activity," he said. However, this and other theories lack "strong clinical and experimental support, and none is totally acceptable as the mechanism by which all attacks of pancreatitis are initiated in the alcoholic."

Coronary Prevention Project Visits Congress



Dr. John LaRosa, left, director of Coronary Prevention Project at George Washington University Medical Center, takes blood pressure of Rep. Leo J. Ryan during coronary risk factor testing of House and Senate members, sponsored by Rep. Walter E. Fauntroy and Senator Charles M. Mathias.

the federal government will have to step in."

In summing up the causes of so many recent suits against physicians, Dr. Egeberg listed the following points: ● Advances in Medicine. Announcements of these have created "an unduly hopeful image of what doctors can do. Some think doctors can interfere with the laws of nature. Ironically, the more advanced the specialty, the greater the danger that a patient will be disappointed."

● Specialization. Specialists may see a patient only a few times in an atmosphere not necessarily conducive to good rapport and understanding. "The specialist is the expert, but many have forgotten they are dealing with a person."

● Change in public attitude. Partly from advances in medicine, partly from news of other malpractice suits, "many people have developed the attitude: 'Maybe I'm missing something.'"

● Physician affluence. "The physician's average income in 1943 was \$3,000. Today people see doctors as pretty damn well off, which they are. This has created a lack of sympathy for them as

a group. They are also a powerful group."

● Insurance. "Patients know doctors are insured into the millions."

● Legalities. "Long-tail liability, abuse of *res ipsa loquitur*, changes in legal trends generally, have increased insurance premiums and raised the cost of health care."

● Attorney fees. The number of suits, as well as the average judgment, is going up 10 per cent a year. "Public expectation is constantly excited."

● Image of perfection. "Many doctors won't admit they made a little mistake or had an accident, especially in hospital settings. In addition, the more sophisticated the techniques, the more opportunity for a slip-up that may turn into a catastrophe."

Dr. Egeberg described federal plans to look more closely at the five or six million unexpected incidents that occur annually in hospitals. "The insurance reports don't tell us enough," he said. "We want to find out more about what actually caused these little accidents, who was to blame, and what was done about it."

Pediatrician-Internist Team Plan Founders

Medical Tribune Report

STANFORD, CALIF.—"A tremendous number of unforeseen problems" will force the termination next July—at least in its present form—of an unusual primary care residency program at the Stanford University School of Medicine.

These problems, explained Dr. Count Gibson, who is chairman of the Department of Family, Community, and Preventive Medicine, have sent him back to the drawing board to design an alternative program for the one which, as presently set up, brings together residents in pediatrics and internal medicine to work in pairs to provide primary health care for a panel of families over a three-year period.

4 Residents in Program

Four residents have been involved in the program, which began last July and is centered in a nearby community health center, rather than the hospital's outpatient departments.

Dr. Gibson sees the problems, frustrating though they have been, as "challenges which require response and solution."

He identified and described some of the major problems which have led to termination of the present program:

Although the heads of the departments of pediatrics and internal medicine supported the collaborative project, no model for the kind of "diadic relationship" proposed existed among faculty members. It proved difficult to develop a working relationship among the residents which did not already exist among faculty members to some degree.

Primary care residents were also part of regular residency programs and "were pulled and tugged away from primary care commitments."

Problems at Health Center

Vacation schedules, for instance, were woven in with the schedules of other internal medicine and pediatrics residents so that one or another of the primary care residents was on vacation for four of the program's first six months.

Also, the chiefs of in-patient services through which the residents rotated have been reluctant to release the primary care residents for a half day to allow them to follow their panel of families, since "the resident on a sophisticated medical ward has become a crucial part of the functioning of the ward."

And some of the rotations were up to 25 miles away from Stanford, creating additional time problems for the primary care residents with their extra commitment.

The community health center where the primary care training is based has had a number of organizational and governing problems, "which might be challenging and stimulating during a six to eight week rotation but don't provide the stable base needed for the training environment of a resident over a three year period."

The members of the community served by the center were not accustomed to the family-centered approach to primary health care. Family members saw no need to come when they

were not sick and were reluctant or found it difficult to bring in an entire family, sick or well.

Also, the most convenient time for an entire family to come was after 5 p.m. when the regular staff of the center was gone and no assistance was available from technicians, social workers, dentists, and others.

A resolution of these problems will produce a new approach to primary care training, Dr. Gibson predicted. He plans to recommend the development of a family practice program, based in a community institution so that the program can be "person, family, and community centered."

The present primary care residency brought together two of the elements Dr. Gibson believes are concerned with primary care, as a pediatrics resident worked with an internal medicine resident in a community health center.

But while the program involved the traditional medical school departments and the community medicine/consumer movement, it did not involve the family practice movement, the third of the "separate and distinct, but interacting" groups involved in primary care, he said.

'Peculiarities' in Training

Although many internists and pediatricians consider themselves primary care specialists, Dr. Gibson maintained that some "peculiarities" in their training make them ill-equipped to provide primary care. He defined primary care as a continuous, broad relationship between patient and physician, not confined to a particular disease but encompassing such elements as early diagnosis, disease prevention, the promotion of health, assistance in convalescence and provision of comfort to the dying.

"The taching hospital, which was the incubator for the modern science of medicine, has produced a group of highly educated, hospital-oriented professionals whose specific focus on the lesion has given rise to more and more subspecialties and has produced a

steady drop in the number of professionals interested in primary care," he said.

The training of internists, for instance, is hospital-based and focused on the diseases, not the person, he explained. And, although half of the problems encountered in primary care are emotional, internists have little training in dealing with emotional problems, and they have none in the growth and development of children and adolescents, he said.

Pediatricians do have some training in dealing with emotional problems but they don't deal with these in a family setting for they give little attention to the father and none to the elderly, Dr. Gibson continued.

Since antibiotics and immunization have changed the type of care provided by pediatricians, "the monotonous aspects of office practice and low financial rewards are making pediatricians an abandoned specialty," he added.

Wearable Tonometer



A plastic ring containing a small pressure transducer that can be worn under the eyelid to monitor eyeball pressure has been developed at the University of Utah. The new system was developed to aid in the research and treatment of glaucoma.

Externally Chargeable Pacer Going Smoothly After 2 Years

Medical Tribune Report

BALTIMORE—The first patient in whom a transcutaneously rechargeable heart pacemaker developed at Johns Hopkins University was implanted has just completed her second year of successful use without complications or the necessity of a reimplant, according to a group of investigators here.

The pacemaker, which is said to be designed to last the patient's lifetime and is smaller and lighter than conventional units, has so far been implanted in over 1,200 patients, said the team, associated with the Johns Hopkins Applied Physics Laboratory.

Only two of the units have failed to date: one suffered a transistor failure and one suffered a seal failure, both without patient injury.

Dr. Kenneth B. Lewis, Assistant Professor of Medicine, Johns Hopkins School of Medicine, who was medical

director for the pacer's development, said that he now implants it in more than 90 per cent of his patients who require pacemakers, "all of whom are successfully recharging at home."

'A Very Simple Process'

According to Robert E. Fischell, technical director of the pacemaker project at the Laboratory, recharging the device is "a very simple process which has been accomplished by patients as old as 93 and children as young as three." Recharging, he explained, takes about one hour each week or four hours each month. No sensation is felt by the patient, who may recharge while reading, watching television, or even sleeping, he said.

Pacemaker Systems, Inc. of Sylmar, California, licensed by Johns Hopkins, manufactures the unit, now provides a ten-year free replacement warranty.

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CLINICAL NEWS NOTE: "Eventually, I expect there will be a uniform system of reviewing all hospital patients, whether their bills are being picked up by the government or third party private insurers, and irrespective of when or whether we get national health insurance. I don't rule out the possibility that one day outpatients will be covered, too." (Dr. Henry E. Simmons, see page 15.)

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Hospital Computer Converted From a 'Redundant Secretary'

By RALPH COSITAM
Special Tribune Correspondent

TUCSON, ARIZ.—Physicians and computer scientists at the San Diego VA Hospital have devised a system that has turned their computer from a "redundant secretary" into a useful tool that has helped improve patient care in the hospital's surgical intensive care unit.

Dr. A. G. Greenburg of the Department of Surgery, University of California, San Diego, said the new system was designed after an evaluation study show the computer was underutilized "primarily because it was not useful."

"The output of the original monitoring system was ignored by the nurses because they distrusted the data or had to work too hard to obtain that which

they already knew, and rejected by the physicians because it represented information they did not need," he said.

Dr. Greenburg said the new system was designed to provide instruction and advice for all personnel, on all aspects of patient care, while attempting to maximize use of the computer.

"We have developed or implemented programs that are both instructive and advisory. Our objective has been to provide easily obtainable, explicit information about specific problems."

With the new system, given a physiologic subsystem and a particular variable, personnel can find out:

- whether or not the variable is deviant;
- obtain a list of probable causes for the deviation;

- obtain an explanation of the pathophysiology of particular deviants as well as instruction on how to identify a most probable cause; and
- how to correct specific deviants.

The new system resulted in an immediate and sustained increase in computer utilization, Dr. Greenburg said.

"As a result, we have a better educated staff who communicate more effectively, deal with more sophisticated information, and make better decisions with resultant improved patient care."

Dr. Greenburg's co-workers in the development of the computer system were a computer scientist, D. K. McClure; an information systems analyst, R. Fink; J. A. Stubbs, R.N.; and Dr. G. W. Peskin.

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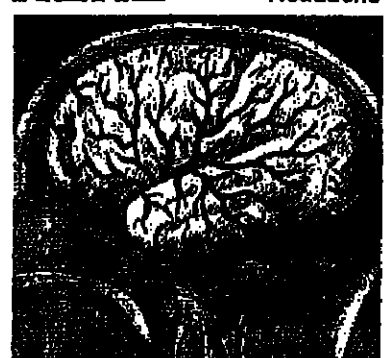
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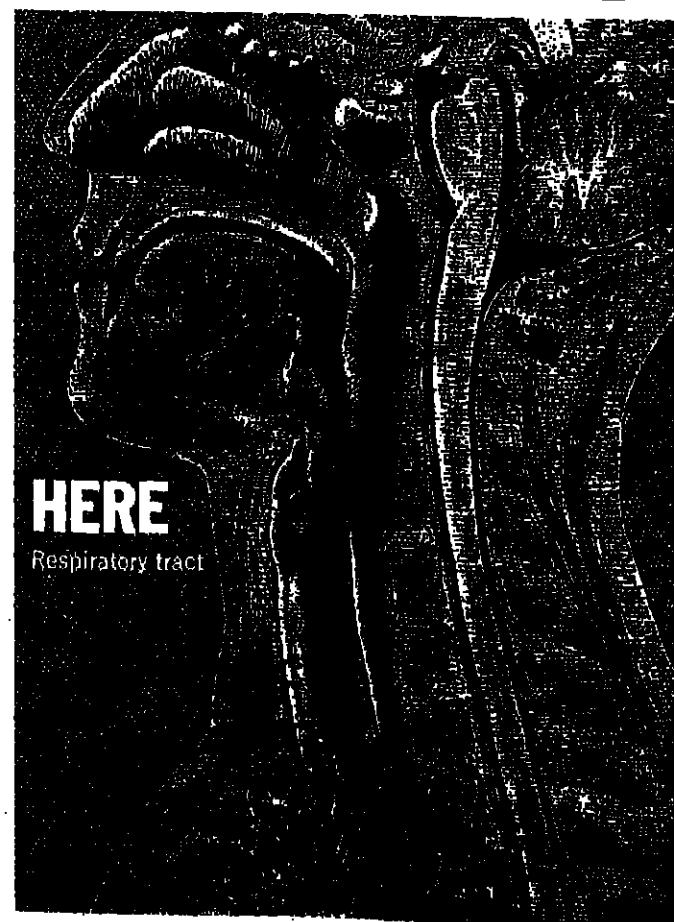
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EDITORIAL CAPSULES

... brief summaries of editorials or comments in current medical and scientific journals.

Provide and Conquer

... our clouded and crazed crystal ball has come up with a prediction of a future move by H.E.W. (as the generic drug thing becomes an established way of life).

"Aux laboratoire, mes amis!"

"With hardly a change in script, the agency can mount the attack. What is the first cry that greets us each day? Health care costs are outrageously high and climbing. Clearly something must be done and the doing can best be accomplished in relation to the ease with which a given area of cost can be identified. To the bureaucratic mind, laboratory service should be a natural. Here is a significant segment of medical care cost for which a monetary figure can be derived from hospital bills, insurance reports, published fee schedules, and the guesses, educated and otherwise, that go into the development of such figures. This can be brought to the public attention with appropriate implications that there must be something unholy about anything that costs that much. . . .

"A standard feature of the bureaucratic approach, gleefully picked up by the Sunday supplements, is the exposure of the unconscionably excessive or inappropriate use of the thing it wishes to control. Someone will "expose" the fact that many laboratory procedures enjoy the sanctity of being called "routine," which often means, in fact, that its value is dubious but which will be interpreted as meaning that no distinct benefit to a particular patient can be demonstrated and it was therefore unnecessary.

"...the laboratory service... is, to the patient, a relatively detached and impersonal activity as compared with his intimate relationship with the physician. We admit to the conviction that it is only the force of this relationship which has spared the clinician from a more complete invasion of his office than already exists. So far, the public has, perhaps unconsciously, resisted this invasion because the physician's private office—or the hospital bed—has been the point of personal contact with the physician, the focus of the private and personal character of the process, the place where he is an individual rather than a unit of contribution. . . .

"In short, the method is relatively simple. Establish control over those services that are peripheral or those with a distinctive social appeal. . . . Don't work directly on old Doc Yak because the public still has kindly feelings for him, but pick off his ancillary services one at a time by agency resolution—a tidier and more effective approach in the long run than legislative confrontation. But the physician has—or should have—the uneasy feeling that when enough of his satellites have been brought under federal control so, to all intents and purposes, will he be. . . ."

(Editorial Comment, David E. Gray, M.D., J. Kans. M.S., 76:42, Feb., 1975)

IN CONSULTATION

What is new and important in food allergy?



The Consultant

DR. CLAUDE A. FRAZIER, M.D., F.A.C.A.
of Asheville, N.C.

Author of *Coping with Food Allergy*, published by Quadrangle Books, New York; Times Publishing Co., New York; and *Insect Allergy*, published by Medical Examination Publishing Co.

I HAVE BECOME intrigued recently by two phases of allergy that are receiving much attention these days—the possibility that allergy to food is far more prevalent than hitherto imagined, and the role of emotional stress in allergy diseases. In a way, the two now and then touch upon the same plane since allergy

to food can produce symptoms so diffuse and so nebulous as to be easily dismissed as being neurotic in origin. And the emotional stress of a patient so summarily dismissed who *knows* he does not feel well, who *knows* that something is wrong, can be imagined. Not only this, but allergy to food can cause some strange central nervous system symptoms such as confusion, irritability, depression, extreme fatigue, poor coordination and the like; all of which may create a bit of skepticism in the attending physician.

It is very important for the physician to know the botanical relationship of foods (cashew nuts, pistachio nuts and mangoes are all in one family) and also where a person may come in contact with a food (peanut oil is sometimes used in cooking doughnuts) and give this knowledge to his patients.

Considering that the ins and outs of food allergy are difficult for the busy non-allergist MD to remember and that the literature is about as diffuse as the symptoms, I took pity on my fellow physicians, not to mention my patients, and stuck everything I could find on the subject in my office between two covers, and called it *Coping with Food Allergy*.

When should food allergy be considered as possibly etiologic in regard to an adult patient's symptomatology?

Since allergy to food can affect any body system and mimic a variety of symptoms ranging from appendicitis to schizophrenia, it should be considered a distinct possibility when differential diagnosis has ruled out more serious contingencies. Especially it must be considered when there is a family history of allergy and when the patient suffers or has suffered other allergies, such as hay fever or colic, as an infant. Physicians beware! Be not quick to decide that yours is a neurotic or hypochondriacal patient. He may simply be allergic to his daily bread!

What constitutes a basic elimination diet and how does one vary it for an individual patient?

Elimination diets must be tailored to individual patients—growing children, sedentary office workers, hard laboring men, etc. Basically, potent allergenic foods such as milk, eggs, wheat, chocolate, nuts, fish and shellfish, berries, peas, citrus fruits and corn are re-

moved, plus foods we can suspect from the patient's history, (or the patient does, since he often knows what doesn't agree) plus foods that appear positive in skin and challenge tests, although the former remain doubtful. Most importantly, vitamin and mineral deficiencies in such a diet must be made up by prescription lest we sink the ship trying to save it.

A physician called me about a patient who developed urticaria after eating mangoes. He later ate cashew nuts, followed by a severe reaction, and still later incurred a more severe reaction by eating pistachio nuts. What about an elimination diet here? The only foods that needed to be eliminated here were mangoes, cashew nuts and pistachio nuts. They are the only foods in this particular botanical family—the Cashew family. If a person is allergic to one food in a botanical family he should eliminate all foods in that particular family.

I have seen several patients severely allergic to peanuts. These patients had been seen by physicians—one by an allergist—and told to eliminate nuts. Peanuts belong to the legume family. These people were continuing to have symptoms as they continued to eat foods in this family. Foods in the legume family should have been eliminated, some of which are acacia, arabic, kidney bean, green bean, lima bean, navy bean, soy bean, wax bean, licorice, black-eyed pea, chick pea, green pea, split pea and tamarind.

I always hand a copy of my book to the patient and tell him to read all about the food to which he is allergic, where it is found and its relationship to other foods.

What is the current status of skin testing to determine food allergy?

Skin testing for food allergy is nowhere near as reliable as it is for inhalants, but I use such procedures on occasion, depending upon the patient and his history. Sometimes correlating skin test results with the history can provide helpful hints of where to go.

What is the current status of desensitization as treatment for food allergy?

I find desensitization results as treatment for food allergy unconvincing and I do not use this procedure except for inhalants and insect stings.

Eubie Blake, at 92, Gives 'Thank You' Concert



Jazz pianist Eubie Blake, 92, was recently admitted to Long Island College Hospital, Brooklyn, for a series of tests. After being pronounced in good health by his physician, Dr. George Liberman, he offered to give a concert for the hospital's staff and ambulatory patients before going home. Steinway Piano Company tuned the piano in the nurses' residence and the concert was on.

What is the role of food additives as allergens?

I agree with Dr. Stephen Lockey that intentional and unintentional (pesticide residues, drug traces, etc.) additives pose an increasing health threat to the allergic. Allergists have already documented cases of patients reacting to such things as butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT), sodium nitrite, the salicylates and their derivatives, bleaching chemicals and chlorine, but there is a great deal we do not yet know about these thousands of chemicals added to our daily fare, including their synergistic effects and whether or not some of them are capable of sensitizing a good part of the population. Let us admit that we are ignorant and act accordingly.

Next In Consultation

Dr. C. J. MARTIN, Director, Institute of Respiratory Physiology, Virginia Mason Research Center, Seattle, Wash., will discuss what's new and important in the diagnosis of diffuse obstructive pulmonary syndromes and the mechanisms involved in causing these syndromes. He will also discuss the relationship between chronic bronchitis, emphysema and tuberculosis as well as the clinical significance of differential aeration and the emptying of different lung compartments. Dr. Martin will also discuss measures that may aid in preventing or arresting the progress of emphysema and pulmonary failure.

Double Form of Gastrin Said To Flaw Radioimmunoassay

Medical Tribune World Service

MEXICO CITY—The usual radioimmunoassay technique of measuring peptide hormones in blood may not be providing an accurate index of their biological activity, the Fifth World Congress of Gastroenterology was told.

The statement was made by Dr. M. I. Grossman, Professor of Medicine, University of California at Los Angeles, in commenting on his work and that of Dr. R. A. Gregory, Professor of Physiology at the University of Liverpool.

Dr. Gregory reported that he determined the true sequence of amino acids in big gastrin in its predominant form of gastrin in blood, and found it has a chain of 34 amino acids, compared with 17 in little gastrin, which predominates in antral tissue. He explained the predominance of big gastrin in blood as due principally to its slower rate of removal.

Dr. Grossman said that he was able to demonstrate the same relationship between the two forms of gastrin in the blood and in the tumor tissue of patients with such disorders as Zollinger-Ellison syndrome.

In commenting on these findings, Dr. Grossman said:

"Actually, a general principle has been discovered. It is that peptide hormones occur in blood and tissue in more than one molecular form and the larger form can be transformed into the smaller form.

"Because of this heterogeneity, and because different forms have different activity, the measurement of the total amount of hormone is not necessarily a valid index of the biological activity of that hormone."

Dr. Grossman also observed that Dr. Gregory's finding has led to a new concept with respect to the relative potency of the two forms of gastrin:

Equimolar amounts of big and little gastrin will produce about the same gastric response. Therefore, based on exogenous doses of hormone, the two forms are about equally potent on a molar basis. However, since the larger form produces a much higher blood level than the smaller one, the "endogenous potency"—that is, the blood level required to produce a given response—is much greater for little gastrin.

Exceptionally well absorbed oral broad spectrum antibiotic may be taken with meals

Larocin® (amoxicillin) achieves high blood and urine levels

Low incidence of diarrhea to date in clinical studies

NUTLEY, N.J.—Roche Laboratories recently introduced an oral broad spectrum antibiotic: Larocin (amoxicillin). Larocin represents a significant contribution to antibacterial chemotherapy, one which will perform effectively in the treatment of a wide range of infections due to susceptible organisms (see chart at right).

Absorption called the key

The key pharmacologic characteristic of Larocin (amoxicillin) is its rapid and efficient absorption from the gastrointestinal tract. Not only is it stable in stomach acid, but the presence of food has no significant effect on the antibiotic's absorption. Thus Larocin may be taken by patients on a convenient t.i.d. schedule without regard to meals. The reconstituted oral suspension and pediatric drops may be added to liquids such as formula, milk, fruit juice or soft drinks for easy administration to small children.

Because of its efficient absorption characteristics, high blood and urine levels of Larocin (amoxicillin) are rapidly achieved. Peak serum levels average 4.2 mcg/ml two hours after a single 250-mg oral dose and 7.5 mcg/ml one hour after a single 500-mg oral dose—both levels approximately twice as high as those obtained with equal doses of ampicillin.^{1,2}

On a multiple-dose regimen, when given every eight hours for 3 days, the lowest mean serum levels of Larocin approximated 1.0 mcg/ml after 250 mg and 1.25 mcg/ml after 500 mg.³ Although the therapeutic range of blood levels for the penicillins is not well established, these results demonstrate that blood levels may be expected to remain above the MIC's for all of the nonurinary pathogens susceptible to Larocin when it is administered at clinically recommended doses (see chart below).

Most of Larocin is excreted unchanged in the urine.³ Average urinary excretion within 6 to 8 hours after oral administration ranges from 40 to 79% for the 250-mg dose and 59 to 79% for the 500-mg dose.^{1,4}

1. Croydon BAP, Sutherland R: *Antimicrob Agents Chemother*—1970, pp. 427-430, 1971. 2. New HC, Winshell EB: *Antimicrob Agents Chemother*—1970, pp. 428-429, 1971. 3. Data on file, Hoffmann-La Roche Inc., Nutley, New Jersey. 4. Leigh DA: *Curr Med Res Opin* 1:10-13, 1972. 5. Boddy GP, Nance J: *Antimicrob Agents Chemother* 1:358-362, 1972.

Hypersensitivity reactions can occur

As with other penicillins, it is anticipated that adverse reactions to Larocin (amoxicillin) will be largely limited to sensitivity phenomena. While anaphylaxis is rare in patients treated with oral

GRAM-POSITIVE	
Alpha-hemolytic streptococci	
Beta-hemolytic streptococci	
<i>Streptococcus faecalis</i>	
<i>Diplococcus pneumoniae</i>	
Nonpenicillinase-producing staphylococci	
GRAM-NEGATIVE	
<i>Haemophilus influenzae</i>	
<i>Escherichia coli</i>	
<i>Proteus mirabilis</i>	
<i>Neisseria gonorrhoeae</i>	

In vitro bactericidal activity

Note: Because Larocin (amoxicillin) does not resist destruction by penicillinase, it is not effective against penicillinase-producing bacteria such as resistant staphylococci. All strains of *Pseudomonas* and most strains of *Klebsiella* and *Enterobacter* are resistant.

penicillins, the possibility must nevertheless be kept in mind. Larocin is contraindicated in patients with a history of penicillin hypersensitivity. SERIOUS ANAPHYLACTOID REACTIONS REQUIRE IMMEDIATE EMERGENCY TREATMENT. (See Warnings section of complete product information, a summary of which appears at right.)

Efficacy demonstrated in many infections

Amoxicillin has been administered successfully to patients with a wide range of commonly seen infections due to susceptible organisms.* Over-all clinical evaluation of amoxicillin therapy was considered a "success" or "improvement" in 1267 of 1850 evaluable cases (68.5%).†

Ages of the 1850 patients studied ranged from under one year to over 80 years. Larocin capsules were administered to 800 patients and oral suspension to the remaining 550. Dosage of the capsules ranged from 250 mg t.i.d. (the most frequently used dosage) to a single 8-Gm dose for the treatment of acute uncomplicated gonorrhea. Dosage of the oral suspension ranged from 50 mg t.i.d. to 250 mg t.i.d., with 125 mg t.i.d. the most frequent. The majority of patients were treated from seven to 10 days. A breakdown by type of infection follows:

Otitis Media: The pathogens most commonly isolated were *Diplococcus pneumoniae* and *Haemophilus influenzae*. Of 130 cases with this diagnosis, 127 (98%) were rated as a "success" or "improvement" after treatment with Larocin (amoxicillin).

Streptococcal Sore Throat: A success rate of 86% (174 of 202 cases) was observed with Larocin against the responsible pathogen, beta-hemolytic streptococci.† The great majority of the 202 patients in this group were children who received the oral suspension.

Other Upper Respiratory Infections: Beta-hemolytic streptococci were the offending organisms for most of the infections in this group, which were diagnosed primarily as pharyngitis, with some cases of tonsillitis and a few cases of sinusitis. A success rate of 82% (56 of 68 cases) was achieved with Larocin.

Lower Respiratory Infections: Treatment with Larocin resulted in "success" or "improvement" in all of the 52 cases in which *Diplococcus pneumoniae* was cultured. *Staphylococcus aureus* was also cultured in 26 of the 98 cases; Larocin showed "success" or "improvement" in 96% (25 of 26 cases). The most common clinical conditions were bronchitis and bronchopneumonia.

Urinary Tract Infections: Cystitis, pyelonephritis and asymptomatic bacteriuria were the most frequent clinical diagnoses in this group. Of the 404 cases evaluated, *Escherichia coli* was cultured in 306 cases and treatment with Larocin resulted in "success" or "improvement" in 284 cases (93%). *Proteus mirabilis* was cultured in 70 patients, with Larocin effective in 67 (96%).

Skin and Soft Tissue Infections: *Staphylococcus aureus* was cultured in 108 cases, with "success" or "improvement" in 104 (96%); while beta-hemolytic streptococci were cultured in 99 cases, with "success" in 97 (98%). Impetigo and abscess were the most frequent diagnoses.

Gonorrhea: Administered as a single 8-Gm oral dose, Larocin showed a success rate of 97% in both males (85 of 88 cases) and females (114 of 118 cases).

*Data on file, Hoffmann-La Roche Inc., Nutley, New Jersey 07110. †"Success" or "improvement" was determined by a combination of clinical and bacteriological criteria. In infections due to beta-hemolytic streptococci and *N. gonorrhoeae*, only successes were included.

Low incidence of side effects reported to date

During the clinical investigations with amoxicillin, all cases treated were evaluated for side effects. No side effects or laboratory abnormalities which would be considered unusual for a penicillin derivative were reported by any of the investigators.

In 2658 total courses of therapy with amoxicillin, therapy was discontinued in only 52 patients

Drug-Related Side Effects Associated with Amoxicillin

Based upon 2658 courses of therapy: 1811 with the capsules and 847 with the oral suspension.

SIDE EFFECT	CAPSULES		SUSPENSION	
	#	%	#	%
Diarrhea	24	1.3	18	2.1
Rash	24	1.3	17	2.0
Nausea	7	0.4	1	0.1
Urticaria	7	0.4	2	0.2
Moniliasis	4	0.2		
Nausea/Vomiting	3	0.1		
Diarrhea/Nausea	2	0.1	4	0.4
Vomiting	2	0.1		
Dizziness	2	0.1		
Colitis	2	0.1		
Nausea/Headache	2	0.1	1	0.1
Rash/Urticaria	1	0.05		
Esophageal Spasm	1	0.05	1	0.1
Stomachache	1	0.05		
Belching	1	0.05		
Drowsiness	1	0.05		
Belching/Numbness/Tingling/Itching	1	0.05		
Fever/Itching	1	0.05		
Difficulty Breathing	1	0.05		
Mucus in Pharynx	1	0.05		
Diarrhea/Urticaria	1	0.05	4	0.4
Diarrhea/Vomiting	1	0.05		
Dizziness/Headache	1	0.05		
Conjunctival Erythema	1	0.05		
G.I. Bleeding	1	0.05		
Abdominal Cramps	1	0.05	1	0.1
Diarrhea/Rash	1	0.05	1	0.1
Rash/Diarrhea/Vomiting	1	0.05	1	0.1
Sore Tongue	1	0.05	1	0.1
Rash/Vomiting	1	0.05		
TOTAL	102	5.6	82	6.1

(1.9%) because of drug-related side effects. Laboratory abnormalities possibly related to amoxicillin occurred infrequently.

In these studies, there was a low incidence of diarrhea reported with amoxicillin capsules—1.7% or 30 of 1811 patients. Especially noteworthy was the low incidence of diarrhea reported with amoxicillin oral suspension—only 2.8% or 24 of 847 patients, significantly less ($p < 0.05$) than the incidence of diarrhea with ampicillin oral suspension (5.3% or 16 of 282 patients).

In breaking down the over-all incidence of diarrhea by age groups, it was found that in the group from 0 to 1 (newborn and 1-year-old infants), 18 of 108 patients receiving amoxicillin oral

suspension developed diarrhea, for an incidence of 12%. This represents over one-half the total number of diarrhea cases seen in the 847 patients treated with amoxicillin oral suspension.

Throughout each of the remaining age categories, starting from age 2 to 10 and in the general grouping from age 11 to 20, the incidence of diarrhea in patients treated with amoxicillin oral suspension ranges from 2% down to 0 in the older groups. There were few cases of diarrhea beyond the age of six.

The incidence of diarrhea with Larocin (amoxicillin) can therefore be expected to be considerably higher in the newborn and infant age groups than in older children, which is true of all antibiotics.

Usual Adult and Pediatric Dosages

INDICATION	STRAIN ISOLATED	ADULT DOSAGE	PEDIATRIC DOSAGE*
Infections of the ear, nose, throat	Streptococci, pneumococci, nonpenicillinase-producing staphylococci, <i>H. influenzae</i>	250 mg t.i.d.	Oral Suspension: 20 mg/kg/day in divided doses t.i.d. Drops: Under 6 kg (13 lbs): 0.5 ml t.i.d.; 6-8 kg (13-18 lbs): 1 ml t.i.d.
Infections of the lower respiratory tract	Streptococci, pneumococci, nonpenicillinase-producing staphylococci, <i>H. influenzae</i>	500 mg t.i.d.	Oral Suspension: 40 mg/kg/day in divided doses t.i.d. Drops: Under 6 kg (13 lbs): 1 ml t.i.d.; 6-8 kg (13-18 lbs): 2 ml t.i.d.
Infections of the genitourinary tract	<i>E. coli</i> , <i>Proteus mirabilis</i> , <i>Strep. faecalis</i>	250 mg t.i.d.	Oral Suspension: 20 mg/kg/day in divided doses t.i.d. Drops: Under 6 kg (13 lbs): 0.5 ml t.i.d.; 6-8 kg (13-18 lbs): 1 ml t.i.d.
Infections of the skin and soft tissues	Streptococci, susceptible staphylococci and <i>E. coli</i>	250 mg t.i.d.	Oral Suspension: 20 mg/kg/day in divided doses t.i.d. Drops: Under 6 kg (13 lbs): 0.5 ml t.i.d.; 6-8 kg (13-18 lbs): 1 ml t.i.d.
Severe infections, or infections caused by less susceptible organisms		500 mg t.i.d.	Oral Suspension: 40 mg/kg/day in divided doses t.i.d.
Gonorrhea, acute uncomplicated gonorrhea and urethral infections (males and females)	<i>N. gonorrhoeae</i>	3 grams—single oral dose	

*Notes: Children weighing more than 8 kg (18 lbs) should receive the appropriate dose of the Oral Suspension: 125 mg or 250 mg/5 ml. Children weighing more than 20 kg should be dosed according to adult recommendations.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Infections due to susceptible strains of the following gram-negative organisms: *H. influenzae*, *E. coli*, *P. mirabilis* and *N. gonorrhoeae*; and gram-positive organisms: streptococci (including *Streptococcus faecalis*), *D. pneumoniae* and nonpenicillinase-producing staphylococci. Therapy may be instituted prior to obtaining results from bacteriological and susceptibility studies to determine causative organisms and susceptibility to amoxicillin.

Contraindications: In individuals with history of allergic reaction to penicillins.

WARNINGS: SERIOUS AND OCCASIONALLY FATAL HYPERSENSITIVITY (ANAPHYLACTOID) REACTIONS REPORTED IN PATIENTS ON PENICILLIN THERAPY. ALTHOUGH MORE FREQUENT FOLLOWING PARENTERAL THERAPY, ANAPHYLAXIS HAS OCCURRED IN PATIENTS ON ORAL PENICILLINS. MORE LIKELY IN INDIVIDUALS WITH HISTORY OF SENSITIVITY TO MULTIPLE ALLERGENS. BEFORE THERAPY, INQUIRE CONCERNING PREVIOUS HYPERSENSITIVITY REACTIONS TO PENICILLINS, CEPHALOSPORINS OR OTHER ALLERGENS. IF ALLERGIC REACTION OCCURS, INSTITUTE APPROPRIATE THERAPY AND CONSIDER DISCONTINUANCE OF AMOXICILLIN. SERIOUS ANAPHYLACTOID REACTIONS REQUIRE IMMEDIATE EMERGENCY TREATMENT WITH EPI-NEPHRINE, ADMINISTER OXYGEN, INTRAVENOUS STEROIDS AND AIRWAY MANAGEMENT, INCLUDING INTUBATION, AS INDICATED.

Usage in Pregnancy: Safety in pregnancy not established.

Precautions: As with any potent drug, assess renal, hepatic and hematopoietic function periodically during prolonged therapy. Keep in mind possibility of superinfections with mycotic or bacterial pathogens; if they occur, discontinue drug and/or institute appropriate therapy.

Adverse Reactions: As with other penicillins, untoward reactions will likely be essentially limited to sensitivity phenomena and more likely occur in individuals previously demonstrating penicillin hypersensitivity and those with history of allergy, asthma, hay fever or urticaria. Adverse reactions reported as associated with use of penicillins: *Gastrointestinal:* Nausea, vomiting, diarrhea. *Hypersensitivity Reactions:* Erythematous maculopapular rashes, urticaria. **NOTE:** Urticaria, other skin rashes and

serum sickness-like reactions may be controlled with antihistamines and, if necessary, systemic corticosteroids. Discontinue amoxicillin unless condition is believed to be life-threatening and amenable only to amoxicillin therapy. **Liver:** Moderate rise in SGOT noted, but significance unknown. **Hemic and Lymphatic Systems:** Anemia, thrombocytopenia, thrombocytopenic purpura, eosinophilia, leukopenia, agranulocytosis. All are usually reversible on discontinuation of therapy and believed to be hypersensitivity phenomena.


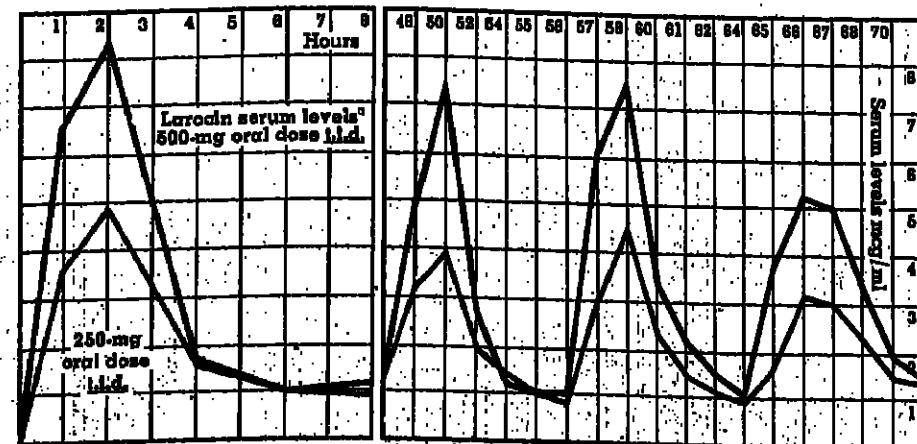
Dosage: Ear, nose, throat, genitourinary tract, skin and soft tissue infections—Adults: 250 mg every 8 hours. Children: 20 mg/kg/day in divided doses every 8 hours; under 6 kg, 0.5 ml of Pediatric Drops every 8 hours; 6-8 kg, 1 ml of Pediatric Drops every 8 hours. **Lower respiratory tract infections and severe infections or those caused by less susceptible organisms—Adults:** 500 mg every 8 hours. Children: 40 mg/kg/day in divided doses every 8 hours; under 6 kg, 1 ml of Pediatric Drops every 8 hours; 6-8 kg, 2 ml of Pediatric Drops every 8 hours. **Gonorrhea (acute uncomplicated gonorrhea and urethral infections)—Males and females:** 3 grams as a single oral dose. **NOTE:** Children weighing more than 8 kg should receive appropriate dose of oral suspension 125 mg or 250 mg/5 ml. Children weighing 20 kg or more should be dosed according to adult recommendations.

Note: In gonorrhea with suspected lesion of syphilis, perform dark-field examinations before amoxicillin therapy and monthly serological tests for at least four months. In chronic urinary tract infections, frequent bacteriological and clinical appraisals are necessary. Smaller than recommended doses should not be used. In stubborn infections, several weeks' therapy may be required. Except for gonorrhea, continue treatment for a minimum of 48-72 hours after patient is asymptomatic or bacterial eradication is evidenced. Treat hemolytic streptococcal infections for at least 10 days to prevent acute rheumatic fever or glomerulonephritis.

Supplied: Amoxicillin as the trihydrate: Capsules, 250 mg and 500 mg; oral suspension, 125 mg/5 ml and 250 mg/5 ml; pediatric drops, 50 mg/ml.

Larocin® (amoxicillin)

an important contribution
to oral broad spectrum
antibiotic therapy

Most Doctors Seen Failing In Dealings With Alcoholics

By JOHN F. HENAHAN
Special Tribune Correspondent

LOS ANGELES—Most physicians are either poorly equipped or reluctant to diagnose and treat alcoholism when they encounter it in patients or in their profession.

That indictment surfaced in various forms at a symposium—held during the California Medical Association's 14th annual session in Los Angeles—devoted to "Alcoholism and Other Drug Dependencies: The Physician's Responsibility."

"Even though physicians may have a common knowledge of the things in their patient's history that may be connected with alcoholism, they hesitate to make the diagnosis and usually wait until the patient goes into the withdrawal syndrome before they do," said Dr. Jude Hayes, medical director of the Tulare County Substance Abuse Program in California.

Strong Clues Noted

Noting that fatty liver, hepatitis, chronic gastritis and a high blood alcohol level, along with a history of marital and job disorders, accidents and other behavioral upsets are strong clues to alcoholism, Dr. Hayes observed that "the physician feels that he just doesn't have the time or counseling skills to deal with an alcoholic patient."

"It is very important that the physician maintains a close and understanding relationship with the alcoholic patient," he urged.

"If it will accomplish nothing else, it will give the patient the realization that he still belongs to the community and that he has not been abandoned to some quasi-governmental agency for treatment."

A physician's reluctance to diagnose and work with the alcoholic patient may also be due to the fact that after he has had some success, the patient frequently goes back to drinking as heavily as ever before.

"The physician then feels that he is somehow responsible for the failure and overlooks the fact that recurrence is the nature of the disease, just as it is in chronic rheumatic disease, coronary artery disease, and cancer," Dr. Hayes said.

Blood Level Data Persuasive

Although it is usually difficult to get the patient to acknowledge that he is an alcoholic, Dr. Hayes believes that the initial step could be taken by confronting the patient with a blood level in the range of 150 mg. per 100 ml. It should be made clear to the patient, he suggested, that even though he does not appear intoxicated at the moment, the blood level is a strong indication that he is an alcoholic and needs help.

"Now that the treatment of alcoholism is being funded by insurance carriers, and a growing number of employers and government agencies now view alcohol as a disease, and not merely a bad habit, the physician is in a better position than ever before to carry out his responsibility to the alcoholic patient," Dr. Hayes said.

Dr. William Lukas, White House

Physician, told a luncheon meeting of the C.M.A. that young doctors are still not receiving enough education in the management of alcoholism.

He suggested that the fact that only 20 per cent of all those now enrolled in Alcoholics Anonymous are there through physician referral, indicates that "we still have a long way to go in this area."

While diagnosis of alcoholism usually associated with some other illness may appear in a patient's record, few are being treated for it, according to Dr. Charles Becker, Head of the Division of Clinical Pharmacology at San Francisco General Hospital.

He cited two surveys taken at San Francisco General over the last several months which indicate that although a group of patients with pancreatitis were diagnosed as alcoholics, the number referred for treatment of alcoholism was "virtually zero."

"In addition," he said, "although the pancreatitis was treated correctly, by failing to consider the alcoholism problem, the physician did nothing to prevent its recurrence. This is clearly a severe deficit in health care delivery."

Dr. Becker said that his technique for treating alcoholics is to use sedatives to detoxify the patient as soon as symptoms of alcoholism are recognizable. Then while the patient is coming back to normal, he administers Antabuse, to keep him away from alcohol during the recovery period.

"The advantage of this type of treatment is that it gives the physician time to build up the proper patient-physician relationship. Then when you have the patient free of alcohol, he should be in a state of mind where you can employ Alcoholics Anonymous, group therapy, individual therapy or just plain human concern."

Special Training Not Needed

"I don't agree that you have to be specially trained to give the proper alcoholic counseling. When a physician says he doesn't have time for the alcoholic, he really means that he doesn't have time to deal with the human aspects of treatment, and when medical practice gets that way, the physician is not rendering overall care to the patient."

If the physician has trouble confronting his alcoholic patients, he may even have more difficulty confronting and admitting his own drinking problems, said Dr. Max A. Schneider, medical director of the Beverly Manor Hospital in Orange, Calif.

For example, he said, it could reduce his objectivity in diagnosing alcoholism in his patients.

"Certainly if a man before me for whom I'm taking a history is drinking a pint a day, and I'm drinking a quart a day, I am not going to be very interested in his alcohol problem. Obviously he couldn't have one, because if he has one, I have one."

"As it is with the general patient, silence is the worst treatment for the alcoholic physician," Dr. Schneider told the C.M.A. symposium, adding that in the case of alcoholic physicians, ignoring a colleague's disease can pose

Now It's 'Cricket' for the Blind to Bicycle



Device called "Cricket," from the sound it emits, invented by a Western Electric engineer, permits a blind person to enjoy bike riding on safe roads or trails. He rides his bike behind another equipped with a "Cricket" (extending from behind the leader's seat). The beep's pitch can be altered so that the blind rider can follow safely from as far as 200 feet or as close as a few feet.

serious problems for himself, his patients, his family and the entire profession.

As an aid to the alcoholic physician Dr. Schneider recommended that every hospital should set up a committee to whom anyone on the staff could submit a report indicating that a physician's drinking was getting in the way of his practice. And when the committee acts, its prime motivation should be therapeutic and not disciplinary, he said.

Dr. Schneider also suggested that local medical societies might follow the "Physician's Hot Line" approach that the Orange County Medical Society has been operating successfully for the last two years. The Hot Line number is known only to physicians and their families and all calls are completely confidential.

"In this way we can refer the alcoholic physician to other physicians who are ready and willing to listen to him and to assist him. At the same time, the process of 'crisis interruption' is immediately set in motion."

Hypnotism Curb Asked

Medical Tribune World Service

TEL AVIV—The Israeli Medical Association has again come out strongly in favor of allowing only licensed physicians to practice hypnotism, following a case in which a stage hypnotist put a 16-year-old girl into a trance and was unable to wake her. The girl was roused nearly a week later by the head of the Israeli Association for Medical Hypnotists.

Anesthesiologist Blocks Marketing of Isoflurane As Possible Carcinogen

Medical Tribune Report

ANN ARBOR, MICH.—A University of Michigan anesthesiologist has blocked release of a new anesthetic gas found to cause tumors in laboratory mice, the university announced.

Dr. Thomas H. Corbett, Assistant Professor of Anesthesiology, reported recently to the International Anesthesia Research Society in Hollywood, Fla., that the anesthetic, isoflurane, with a chemical structure similar to the carcinogen bis(chloromethyl) ether, itself produced a significant incidence of tumors in mice.

Pulmonary adenomas were two to three times greater among isoflurane-anesthetized mice at six months, and three to five times greater at nine months, than they were among non-anesthetized mice, he found.

"Although all anesthetics are screened and tested for other toxic properties before approved for human use, our studies indicate a genuine need to evaluate the possible carcinogenicity of the halogenated ethers and other inhalation anesthetic agents," Dr. Corbett commented.

Manufacturers have agreed to withhold distribution of isoflurane, even though routine protocols and procedures were followed to obtain necessary approvals, the university announcement said.

Behavior Modification a 'Lightning-Rod Issue'

Medical Tribune Report

DALLAS—Behavior modification is a "lightning-rod issue" in mental health, Dr. Bertram Brown, Director of the National Institute of Mental Health, said here.

"Drawn to behavior modification therapy," Dr. Brown said, "are such highly charged issues as fears of mind control and concerns about the treatment of persons institutionalized against their will."

He attributed a portion of the present ethical controversy of behavior modification to its overpopularization in such works as the movie "Clockwork Orange," and to an "incorrect linkage" to other psychiatric techniques such as psychosurgery and chemotherapy.

Dr. Brown spoke to a Symposium on Human Experimentation presented by Southern Methodist University School of Law.

Apart from the obvious misconceptions about behavior modification therapy, he said, there are serious and responsible reasons for some concern about its legal and ethical aspects. The most frequently criticized use of behavior modification, he noted, is its use in altering the behavior of persons



DR. BROWN

who are involuntary participants in therapy.

"The mental health worker who proposes to modify the patient's environment to alter maladjustive behavior can be seen as serving the interest of the institution rather than favoring the right of the person to express his individuality," he said.

"Behavior modification is not a one way method that can be successfully imposed on an unwilling individual," he said. "By its nature, behavior modification will succeed only when the individual is responsive to the therapist and cooperates with treatment programs."

Problems Vary With Settings

Dr. Brown contended that one difficulty in establishing ethical standards for behavior modification is that the problems vary with different settings.

In prison, where the behavioral professional is in the position of assisting in the management of rebellious prisoners, he remarked, the distinctions among therapy, management, and rehabilitation may become blurred.

"Informed consent is clearly meaningful when a normal adult voluntarily seeks such treatment in an out-patient clinic," he said. "With prisoners it's a different matter, and it by no means clear that they are even able to give truly voluntary consent. There are special pressures to participate...."

Myasthenia Gravis Booklet

Medical Tribune Report

NEW YORK—A nine-page "fact book" on myasthenia gravis has been published by the Greater New York Chapter of the Myasthenia Gravis Foundation. The booklet is intended for patients and the public.

A common position at present, he said, is to recommend the elimination of behavior modification programs in prisons, on the grounds that such therapy is coercive. "Yet if constructive programs are eliminated, the opportunity for inmates who genuinely want to participate and who might benefit is denied."

The Mentally Retarded Child

A further evaluation must also be made of informed consent in relation to the child in the mental retardation school, Dr. Brown noted. "What about the mentally retarded child that continuously bangs his head, yet can't give informed consent?" he asked. "There are certain types of behavior modification that could possibly turn him into

a more adapted child but who gives permission? the parents, therapists, who?"

Dr. Brown advised therapists to first evaluate the extent to which the target population can truly give consent, then for the therapist and patient to weigh through a review committee the benefits against the possible risks of treatment.

"This is still a new form of therapy," he said. "It has been fully developed only in the last five years and it is basically built on a foundation of human experimentation."

"Particularly strong is the need for additional research comparing the efficacy of behavior modification methods with that of alternative treatment approaches," he said.



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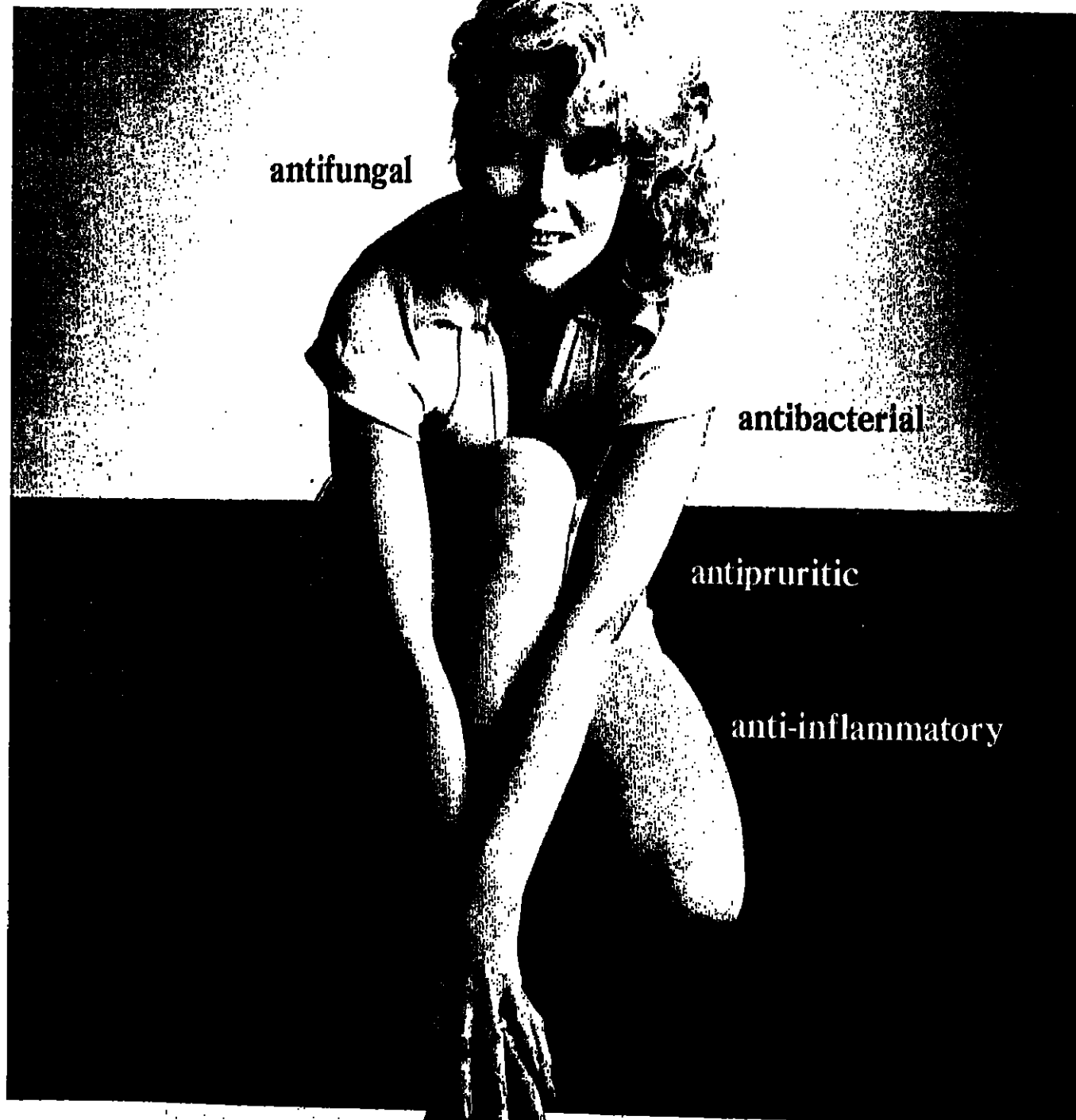


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the bare facts



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It's plain to see that you need more than an ordinary topical steroid to clear a dermatitis infected with fungi or bacteria.

Vioform-Hydrocortisone, with its four-way action, provides the kind of comprehensive therapy many common dermatoses* require.

*This drug has been evaluated as possibly effective for these indications. See brief prescribing information.

Vioform-Hydrocortisone (iodochlorhydroxyquin and hydrocortisone)

INDICATIONS
Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the indications as follows:
"Possibly" effective: Contact or atopic dermatitis; impetiginized eczema; nummular eczema; infantile eczema; endogenous chronic infectious dermatitis; small dermatitis; pyoderma; nuchal eczema and chronic seborrheic dermatitis; external acne urticaria; localized or disseminated neurodermatitis; lichen simplex chronicus; anogenital pruritus (vulvae, scroti, ani); folliculitis; bacterial dermatoses; mycotic dermatoses such as tinea (capitis, corporis, pedis); molluscum contagiosum.
Final classification of the less-than-effective indications requires further investigation.

CONTRAINDICATIONS
Hypersensitivity to Vioform-Hydrocortisone, or any of its ingredients or related compounds; lesions of the eye; tuberculosis of the skin; most viral skin lesions (including herpes simplex, varicella, and varicella).

WARNINGS
This product is not for ophthalmic use.
In the presence of systemic infections, appropriate systemic antibiotics should be used.

Usage in Pregnancy
Although topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use in pregnant females has not been established. Therefore, they should not be used extensively on pregnant patients in large amounts or for prolonged periods of time.

PRECAUTIONS
May prove irritating to sensitized skin in rare cases. If this occurs, discontinue therapy. May stain.

If used under occlusive dressings or for a prolonged period, watch for signs of pituitary-adrenal axis suppression.
May interfere with thyroid function tests. Wait at least one month after discontinuance of therapy before performing these tests. The ferric chloride test for phenylketonuria (PKU) can yield a false-positive result if Vioform is present in the diaper or urine.
Prolonged use may result in overgrowth of non-susceptible organisms requiring appropriate therapy.

ADVERSE REACTIONS
Few reports include: hypersensitivity, local burning, irritation, pruritus, discoloration (unwanted) occurs rarely; topical corticosteroids may cause atrophy of skin at site of application when used for long periods in intertriginous areas.
Warnings
Avoids a thin layer in affected areas 3 or 4 times daily.

HOW TO USE
Cream: 3% Iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing

sterilized alcohol, cetyl alcohol, stearic acid, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of 5 and 20 Gm. Ointment: 3% Iodochlorhydroxyquin and 1% hydrocortisone in a petrolatum base; tubes of 5 and 20 Gm. Lotion: 3% Iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearic acid, trioleate, polyethylene glycol, sorbitan, cetyl alcohol, lanolin, propylene glycol, sorbitan, trioleate, polyethylene glycol, and perfume. Flammable. Vioform-Hydrocortisone, 3% Iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearic acid, trioleate, polyethylene glycol, sorbitan, cetyl alcohol, lanolin, propylene glycol, and perfume. Flammable. Vioform-Hydrocortisone, 3% Iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearic acid, trioleate, polyethylene glycol, sorbitan, cetyl alcohol, lanolin, propylene glycol, and perfume. Flammable.

In water-washable tubes of 1/2 and 1 ounce. Mild Ointment, 3% Iodochlorhydroxyquin and 0.5% hydrocortisone in a petrolatum base; tubes of 1/2 and 1 ounce. Consult complete product literature before prescribing.

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Vioform-Hydrocortisone

(iodochlorhydroxyquin and hydrocortisone)

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C I B A

Wednesday, April 23, 1975

MEDICAL TRIBUNE

11

The Only Independent Weekly Medical Newspaper in the U.S.

Medical Tribune

and Medical News
Published by Medical Tribune, Inc.

Malpractice Insurance

THE BILL ON malpractice passed by the Indiana State House of Representatives at the time of this writing (see page 2) and revised by that state's Senate merits the attention of all U.S. physicians. It is supported by the Indiana State Medical Association and is distinguished by the formation of pre-trial screening panels to hear and advise on all malpractice cases.

The panels are to include three physicians who will present their findings to a court of law and are expected successfully to eliminate "nuisance" cases, permitting reliable actuarial figures to be developed in time for determining premiums to be paid by physicians. Unfortunately, so far as we can tell, although the Indiana bill augurs improvements in the future, it does not solve the problems in those states where insurance companies are in the process of discontinuing all malpractice insurance.

An article on "no-fault malpractice insurance" in the March, 1975, issue of *The Western Journal of Medicine* by Dr. J. W. Bush and coworkers at the University of California, San Diego, also ignores the problem of immediate discontinuance of malpractice insurance and addresses itself to the essential problem of how to decide malpractice cases. It dismisses no-fault insurance as unsatisfactory or, rather, inapplicable in malpractice cases and, instead, opts for "a probabilistic framework for analyzing the issues of malpractice insurance," in the belief that

this will provide "the framework for a more efficient and equitable compensation system divorced from the concept of individual faults."

Dr. Bush and his colleagues consider the usual malpractice case in which medical negligence is claimed. They show how in any particular case calculations can be made of the likelihood of untoward outcome on the basis of the procedure chosen by the defendant physician as compared with the likelihood of untoward outcome of "acceptable" treatment. Based on such calculations, a coefficient of causality can be determined, its statistical significance evaluated, and awards would be made that would assure "that all plaintiffs with some merit to their claims, recognizing that unacceptable practice was present, would be compensated in proportion to their merit instead of all or nothing."

This plan calls for review of cases by "some specialized branch of the judicial system, like Workmen's Compensation, or perhaps by the Professional Standards Review Organizations currently being established." This differs markedly from the proposed Indiana pre-trial screening panels.

This plan seeks to eliminate the vagaries of a jury trial where, as Dr. Egeberg notes, issues that are not at all germane lead to a jury's decision and the size of an award.

This is probably the shape of the future—but what of the present moment?

Versatile Aspirin

NUMBER OF editorials in MEDICAL TRIBUNE have referred to the versatility of aspirin as an active drug over and beyond its antipyretic, analgesic and antiinflammatory effects. It appears to be an inhibitor of platelet aggregation. It has been shown to inhibit leukocyte migration into inflamed areas and to suppress the multiplication and proliferation of lymphocytes in response to phytohemagglutinins and other stimulating mitogens. These are responses that are sometimes therapeutically desirable, as in the so-called autoimmune diseases.

Now a report in the March 24 issue of *J.A.M.A.* by Dr. Edith D. Stanley and her colleagues presents evidence

that aspirin treatment of volunteers challenged with rhinovirus increases the rate of virus shedding as compared with placebo-treated subjects. The aspirin modestly improved the local symptoms of the rhinovirus infection but the investigators speculate that if this encouraged staying on the job, it would also be more likely to increase spread of the virus to contacts. They add, "Whether the enhanced rhinovirus replication has any adverse effects on the individual host is not known, but it is possible."

It goes without saying that this merits further study yet it does not seem likely that use of this remarkable agent is likely to diminish.

Congenital Cytomegalovirus Infection

CLINICAL QUOTE: "CMV-IgM antibody was present in the cord serum of 1 in 163 general deliveries of infants born to parents of all social classes... occurred twice as often among the lower social classes... was associated with variable intellectual and neurological deficits... is a significant cause of profound deafness... Prediction of school failure in CMV-IgM positive children was made

in 16/30 (53.3 per cent) children tested. Although the probability of school failure was not observed in CMV-IgM positive children from middle and higher socio-economic groups, one cannot conclude... that there has not been some diminution in intellectual potential in these children." (Dr. James B. Hanshaw, Symposium on Infections of Fetus and Newborn Infant, see page 1.)



"A nervous breakdown? I can't possibly squeeze it in."

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LETTERS TO TRIBUNE

Costs and Blue Cross

Although your article on the latest criticism of Blue Cross-Blue Shield (MT, Mar. 5) is similar to what is being published elsewhere, it seems to reflect more the politics of the situation than the actual facts. It is fashionable but demagogic to blame Blue Cross and other insurers for failure to "control" health care costs. The price of care keeps going up primarily because of rising standards, not because of incompetence or greed on the part of hospitals. Despite an occasional well-publicized abuse of public trust, it is obvious that the vast majority of these institutions do an admirable job of providing the best possible care with the funds available.

I'm not sure it was wise to depend on Herbert Denenberg as a major source for your article. His penchant for conjuring up devils and rendering difficult issues in stark black and white reminds one of the late Senator Joseph McCarthy.

It may be that the United States is approaching a genuine crisis as our rapidly expanding visions of ideal medical care outpace our ability to provide it for all our people. As a nation we may have to make some agonizing choices between ideal treatment for patients with such problems as end-stage renal disease or metastatic cancer and everyday medical care for the large population groups who presently get little of it. Unfortunately, it seems likely that such decisions will be made in the arena of national politics, a prospect that gives one little hope that they will be made rationally. Who can imagine a public official saying "I wish you doctors would quit inventing all those new treatments. They are nice, but dammit, we can't afford them."

ROBERT D. GILLETTE, M.D.
Huron, Ohio

Protecting the Patient

In your editorial of March 19, 1975, "A.M.A. sues to protect patients," you said that A.M.A. has "... at long last" begun to stand up to government intervention into the doctor-patient relationship; and implied that A.M.A. is opposing P.S.R.O.

A.M.A. has filed suit against the Utilization Review rules promulgated in the *Federal Register*, not against

P.S.R.O. While both accomplish the same purpose, A.M.A. delegates have approved of P.S.R.O., and A.M.A. has received a great deal of money to study methods of implementing P.S.R.O. The official policy of A.M.A. is thus schizophrenic; while approving the entire P.S.R.O. package, A.M.A. ostensibly disapproves of a portion of the same package.

A.M.A. is also a little late. The American Council of Medical Staffs filed suit several weeks before A.M.A. against H.E.W. Utilization Review Rules. C.M.S. is also Amicus Curiae in the A.A.P.S. suit against P.S.R.O.

It would appear that the Council of Medical Staffs and A.A.P.S. are more interested in preserving the "historic rights of patients."

Incidentally, C.M.S. also has published the most exhaustive and authoritative review of Adverse Drug Reactions and Generic Prescribing.

Because we're no. 2, we apparently cannot command the attention which no. 1 does.

KENNETH A. RITTER, M.D.
American Council of Medical Staffs
New Orleans

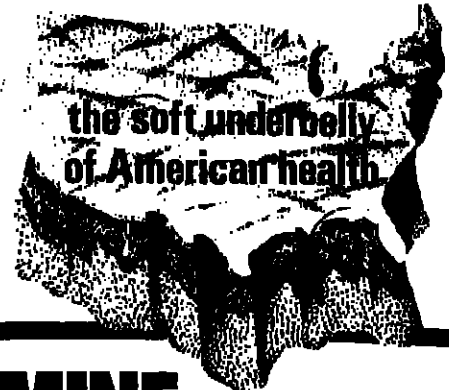
Ascent of Man

An extraordinary coincidence occurred yesterday. I read Dr. Sackler's comments "One Man... and Medicine" (MT, Mar. 26) and the same evening I listened to Dr. Bronowski on the TV program "Ascent of Man." They must have been collaborators! The same theme was expressed in his article and on TV—the relation of science to humanity, or rather the humanistic aspects of scientists.

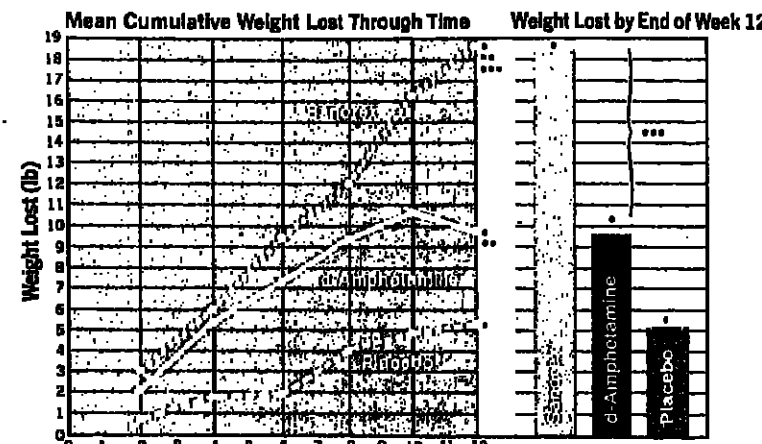
I still believe that one of the most remarkable humanistic events in the history of mankind occurred during World War II—the first collective awareness of social consciousness of scientists who were concerned with the development of the atomic bomb. This stood in sharp contrast to other scientists who, with complete indifference, subjected human beings to painful experiments often ending fatally. Perhaps the shock of this indifference had something to do with the birth of social consciousness of the atomic scientists.

CARL S. ALEXANDER, M.D.
Professor of Medicine
Veterans Administration Hospital
Minneapolis, Minn.

MAZINDOL® (MAZINDOL) TABLETS, 1 mg and 2 mg.

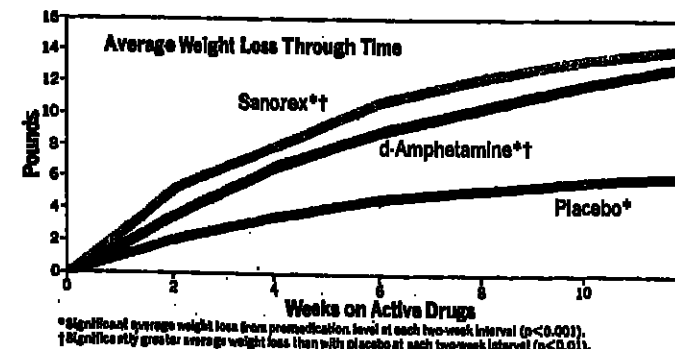


AS EFFECTIVE AS d-AMPHETAMINE



In a double-blind study¹ of 40 obese patients (all of whom completed the study), Sanorex (1 mg t.i.d.) was more effective than either placebo or d-amphetamine (5 mg t.i.d.) in helping patients lose weight.

The 14 patients on Sanorex experienced a substantially greater mean weight loss—1½ to 2 lb/wk, as compared with 1 to 1½ lb/wk for the 14 d-amphetamine patients—throughout the 12-week phase of active medication. After the sixth week, the superiority of Sanorex became increasingly evident. And as treatment progressed, so did weight loss in patients on Sanorex—whereas after the tenth week, patients on d-amphetamine began to regain some weight.



In a double-blind study² of 93 obese patients (all of whom completed the study), 30 patients received Sanorex (1 mg t.i.d.), 31 received placebo, and 32 received d-amphetamine (5 mg t.i.d.).

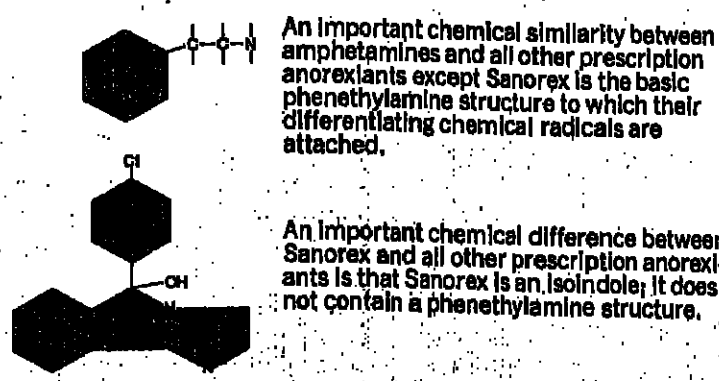
During the 12-week phase of active medication, patients on Sanorex lost an average of 14.1 lb, compared with 13.1 lb for d-amphetamine patients and 5.6 lb for placebo patients. Throughout the active medication phase, 63% of patients on Sanorex lost more than 1 lb/wk, compared with 38% of the d-amphetamine group and 29% of the placebo group.

BUT WITH CERTAIN DIFFERENCES

Although the pharmacologic activity of Sanorex and that of amphetamines are similar in many ways (including central nervous system stimulation in humans and animals, as well as production

of stereotyped behavior in animals), animal experiments suggest that there are differences.* Sanorex also differs in basic chemical structure from amphetamines and all other prescription anorexants.

Different Chemical Structure



Different Neurochemical Action

Action of d-Amphetamine In animal studies, d-amphetamine (like intake of food) activates afferent neurons leading to appetite centers in the hypothalamus. Resulting release of norepinephrine activates the receptor neurons. Unlike food, however, d-amphetamine also suppresses norepinephrine synthesis. Thus, increasingly larger doses of d-amphetamine become necessary to produce an effect.

Action of Sanorex (mazindol) After intake of food stimulates the release of norepinephrine from the afferent neuron, Sanorex blocks its re-uptake without disturbing normal synthesis and release.*

*The significance of these differences for humans is uncertain.

Simplicity and Flexibility of Dosage

Simple one-a-day dosage is facilitated by 2-mg tablets (taken 1 hour before lunch).

New flexibility (for the patient in whom 1 mg t.i.d. is preferred) is now facilitated by new 1-mg tablets (taken 1 hour before meals).

For Brief Summary, please see facing page.

SANOREX® (MAZINDOL)®

References

1. Kornhaber A: Problems and current concepts in the treatment of obesity. Scientific Exhibit presented at the New York State Academy of Family Physicians, 25th Annual Scientific Convention, Albany, N.Y., May 8-10, 1973.
2. DeFallo EA, Chaykin LB, Cohen A: Double-blind clinical evaluation of mazindol, dextroamphetamine, and placebo in treatment of exogenous obesity. *Ann Ther Res* 15:358-366, July 1973.
3. Vernace BJ: Practical considerations for managing obese patients: initial interview and effective treatment in the office. Scientific Exhibit presented at the American Medical Association, 27th Clinical Convention, Anaheim, Calif., Dec 1-4, 1973.

Indication: In exogenous obesity, as a short-term (a few weeks) adjunct in a weight reduction regimen based on caloric restriction. The limited usefulness of agents of this class should be measured against possible risk factors.

Contraindications: Glaucoma; hypersensitivity or idiosyncrasy to the drug; agitated states; history of drug abuse; during, or within 14 days following, administration of monoamine oxidase inhibitors (hypertensive crisis may result).

Warnings: Tolerance to many anorectic drugs may develop within a few weeks; if this occurs, do not exceed recommended dose, but discontinue drug. May impair ability to engage in potentially hazardous activities, such as operating machinery or driving a motor vehicle, and patient should be cautioned accordingly.

Drug Interactions: May decrease the hypotensive effect of guanethidine; patients should be monitored accordingly. May markedly potentiate pressor effect of exogenous catecholamines; if a patient recently taking mazindol must be given pressor amine agents (e.g., levaterenol or isoproterenol) for shock (e.g., from a myocardial infarction), extreme care should be taken in monitoring blood pressure at frequent intervals and initiating pressor therapy with a low initial dose and careful titration.

Drug Dependence: Mazindol shares important pharmacologic properties with amphetamines and related stimulant drugs that have been extensively abused and can produce tolerance and severe psychological dependence. Manifestations of chronic overdosage or withdrawal with mazindol have not been determined in humans. Abstinence effects have been observed in dogs after abrupt cessation for prolonged periods. There was some self-administration of the drug in monkeys. EEG studies and "liking" scores in human subjects yielded equivocal results. While the abuse potential of mazindol has not been further defined, possibility of dependence should be kept in mind when evaluating the desirability of including the drug in a weight-reduction program.

Usage in Pregnancy: In rats and rabbits an increase in neonatal mortality and a possible increased incidence of rib anomalies in rats were observed at relatively high doses. Although these studies have not indicated important adverse effects, the use of mazindol in pregnancy or in women who may become pregnant requires that potential benefit be weighed against possible hazard to mother and infant.

Usage in Children: Not recommended for use in children under 12 years of age.

Precautions: Insulin requirements in diabetes mellitus may be altered. Smallest amount of mazindol feasible should be prescribed or dispensed at one time to minimize possibility of overdosage. Use cautiously in hypertension, with monitoring of blood pressure; not recommended in severe hypertension or in symptomatic cardiovascular disease including arrhythmias.

Adverse Reactions: Most commonly, dry mouth, tachycardia, constipation, nervousness, and insomnia. **Cardiovascular:** Palpitation, tachycardia. **Central Nervous System:** Overstimulation, restlessness, dizziness, insomnia, dysphoria, tremor, headache, depression, drowsiness, weakness. **Gastrointestinal:** Dryness of mouth, unpleasant taste, diarrhea, constipation, nausea, other gastrointestinal disturbances. **Skin:** Rash, excessive sweating, clamminess. **Endocrine:** Impotence, changes in libido have rarely been observed. **Eye:** Long-term treatment with high doses in dogs resulted in some corneal opacities, reversible on cessation of medication; no such effect has been observed in humans.

Dosage and Administration: 1 mg three times daily, one hour before meals, or 2 mg per day, taken one hour before lunch in a single dose.

How Supplied: Tablets, 1 mg and 2 mg, in packages of 100.

Before prescribing or administering, see package circular for Prescribing Information.

MAZINDOL PHARMACEUTICALS, EAST HANOVER, N.J. 07930

Congenital CMV Infections Linked to Low IQ, Deafness

Continued from page 1

Medicine and sponsored by the National Foundation-March of Dimes.

Describing the findings on intelligence levels, the investigator explained that IQ levels of the positive children were compared with those of two other groups: an equal number of controls matched for age, sex, race, birth weight, and social class (Hollingshead classification); and 44 children born immediately after the birth of an infant with CMV-IgM antibody in the cord serum.

All told, 20 of the children had an IQ below 90, Dr. Hanshaw said. Of this number, 12 were in the CMV-IgM positive group while only six came from the matched control group and two from the random controls.

Of the seven children who had an IQ below 80, all had been CMV-IgM positive at birth.

Abnormalities in 16 of 44

Dr. Hanshaw noted that 16 of the 44 positive children (36.3 per cent) showed intellectual, behavioral, neurological, or sensory abnormalities "sufficient to predict the need for special education not available in the usual school setting."

By contrast, school failure was predicted in six of the matched controls and two of the random-control children.

Bilateral hearing loss was found in five of the positive group, the investigator said, and three of these children are profoundly deaf. Only one child in each of the control groups had bilateral loss.

The effect of social class on congenital CMV infection was evident, Dr. Hanshaw commented. Although the majority of the more than 8,000 infants tested were from middle-class families, CMV-IgM antibody was found twice as often among infants born to parents in the lower socioeconomic groups.

Also, all 16 of the antibody-positive children with abnormalities "precluding adequate performance" in a normal school setting came from the lower socioeconomic groups. But this finding, in Dr. Hanshaw's view, does not rule out the possibility that congenital CMV infection may diminish the intellectual potential of children from middle and upper socioeconomic groups.

Available Drugs Toxic

In a second report on CMV, Dr. David J. Lang, of Duke University Medical Center, labelled it "the infectious agent most frequently associated with congenital injury, and damage" and cautioned that chemotherapy of such infections "has been disappointing thus far."

Dr. Lang cited present estimates that about 40 to 50 per cent of white, middle-class women in this country are CMV antibody positive by the time they reach childbearing age, while higher rates of antibody prevalence—and earlier acquisition of infection—have been reported among blacks and people of low socioeconomic status. Approximately one per cent of all five-born infants are congenitally infected

and at least 10 per cent of these eventually manifest significant damage.

The drugs now licensed for experimental trials in man are associated with significant toxicity, the investigator said. As a result, he believes it is not likely "in the foreseeable future" that a prospective therapeutic trial will be made among congenitally infected infants who seem reasonably healthy.

A further problem cited by Dr. Lang is the difficulty of making a clinical identification of a primary CMV infection during pregnancy. It appears most often as a mild, undifferentiated or subclinical illness, he pointed out, and the clinical syndromes "are even less well defined than those accompanying rubella."

Although Dr. Lang agrees that a CMV vaccine is needed, he warned that many questions must be resolved before more clinical trials of the present experimental vaccine could be justified.

There is no precedent for the "deliberate administration of a virus that may establish a latent or persistent infection," he said. Additionally, there are no criteria established for attenuation of CMV—and these are hard to determine "when the wild-type virus usually induces very mild illnesses."

Other questions posed by Dr. Lang: Is the apparent attenuation achieved after tissue culture passage liable to in-

Computer Placement



Minnesota communities affected by shortages of medical personnel, many in isolated areas near the Canadian border, are being helped by a computer placement service at the University of Minnesota. The service matches economic base, recreational facilities, and population of towns with the preferences of graduating medical students. Above, a third-year student looks over the list of communities wanting a doctor.

crease the likelihood of the persistence of CMV and/or the neoplastic transformation of infected cells? Would a "killed virus" vaccine interrupt patterns of CMV transmission?

"In spite of the pressing need for control of CMV," he concluded, "insufficient information exists relevant to natural patterns of virus spread and control to permit the evaluation in man of modified CMV strains at this time."

Beneficial Results Reported With Splenic Artery Ligation

By RALPH COSHAM
Special Tribune Correspondent

TUCSON, ARIZ.—A University of Arizona surgeon has revived a 95-year-old procedure to reduce the need for—and risk of—splenectomy in hypersplenic patients.

Dr. Charles L. Witte, of the University of Arizona College of Medicine, told the annual meeting of the Society of University Surgeons that he has obtained beneficial results with splenic artery ligation in selected patients with hypersplenism, certain blood dyscrasias, and cirrhosis of the liver.

Dr. Witte said the advantage of splenic artery ligation is that it reduces the activity of the spleen without total destruction of the organ.

Noting that total splenectomy increases the risk of infection, he said it has not yet been demonstrated that the spleen's protective function is retained after splenic artery ligation, "but that is what we are trying to show."

Dr. Witte and co-workers are injecting rats with sheep erythrocytes, the antibody to which is produced in the spleen.

"Splenectomized rats will not produce the antibody," he said. "We are hoping that the ligated ones will."

In previous experiments, he went on, splenic artery ligation reversed hematologic abnormalities in Sprague-Dawley rats in which hypersplenism had been artificially induced.

The procedure was then tried in twin boys with hereditary spherocytosis and

a young girl with idiopathic thrombocytopenic purpura (ITP).

"These patients had a reduction in their functional splenic mass," Dr. Witte reported, "and in the hereditary spherocytosis, the most important thing is that the blood hematocrit and reticulocyte count have been stable for almost 18 months."

Immediate Rise in Platelets

"In the patient with ITP we had an immediate rise in platelet count, bounced around for a while, but 16 months postoperatively it was normal."

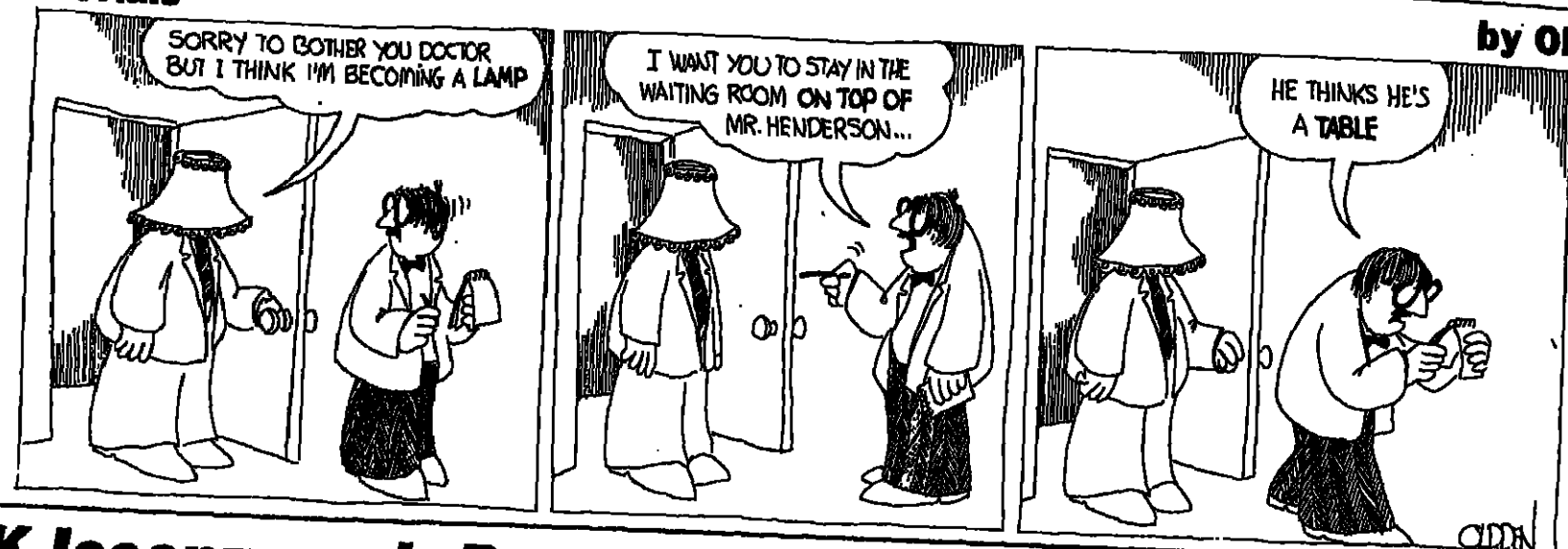
"One can get spontaneous remission in ITP," he said, "but the fact is this girl had symptoms of bruisability and nosebleeds and low platelet counts for a year before we ligated the artery."

Among the other patients were three with cirrhosis of the liver and splenomegaly with various kinds of cytopenia, Dr. Witte said.

Splenic artery ligation produced—in two of the patients—clinical, symptomatic, and blood count improvements, he said, adding that "it may not be as good as if we had done a splenectomy, but it's good enough to produce a remission and they still have the advantage of the splenic veins in that area."

"Putting the ligature too close to the origin of the splenic artery rather than at the end may be why earlier efforts with this procedure failed," Dr. Witte commented. "They may have been getting tremendous collaterals without even knowing it."

Clinical Trials



by Olden

CPK Isoenzyme Is Reported Good Index of Size of Infarct

Continued from page 1

The studies of infarct size were made by a new kinetic fluorimetric procedure developed at the St. Louis center that can assay MB CPK quantitatively, according to Dr. Robert Roberts. Estimates were based on hourly changes in serum values of the isoenzyme.

With uncomplicated infarction, he commented, the isoenzyme released into serum paralleled total CPK released. Estimates of infarct size calculated from MB CPK and from total CPK agreed closely, with a correlation coefficient of 0.97.

Complicated-Infarction Studies

Dr. Roberts said the special usefulness of the quantitative assay of MB became apparent in studies of patients with complicated infarction. In such cases, he noted, realistic estimates of infarct size based on total CPK are not possible because noncardiac CPK will have been liberated into the circulation. It was found that infarct size esti-

mated from serial changes in the serum isoenzyme activity was significantly less than the size estimated from total CPK. The investigators conclude that the isoenzyme approach permits a reliable evaluation of the extent of infarction in patients with shock accompanied by release of CPK from sources besides the heart.

Describing assays of the isoenzyme following cardiac catheterization, Dr. Philip A. Ludbrook reported that blood samples for determination of total CPK and MB isoenzyme activity were obtained from 50 patients immediately before the procedure and every two hours thereafter for 24 hours.

None of these patients developed clinical or ECG evidence of myocardial injury or infarction.

For purposes of comparison, the same determinations were made on 50 patients with recent transmural myocardial infarction and on 20 hospitalized controls with no form of cardiac disease.

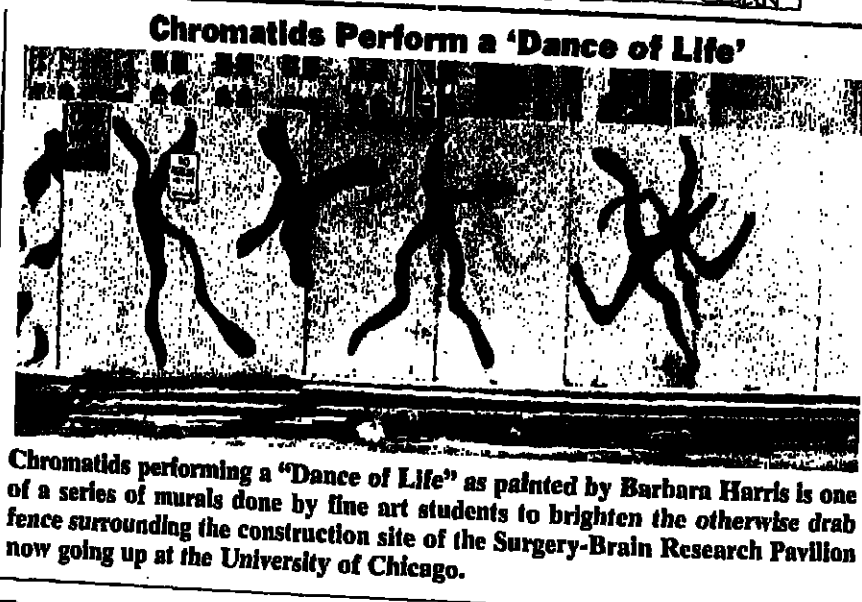
Total peak CPK activity was significantly elevated in three-fourths of the 50 patients undergoing catheterization and mildly increased in the rest, Dr. Ludbrook said.

"However, MB CPK activity remained within the normal range in all cases," he reported, "indicating that myocardial damage did not occur and that increased total CPK activity did not reflect release of enzyme from the heart."

In the 50 patients with documented myocardial infarction, peak total CPK activity was also significantly elevated—reaching levels considerably higher than those observed in the catheterization group. But in sharp contrast to the MB findings in cardiac catheterization patients, all 50 of the infarction patients showed significantly elevated MB CPK isoenzyme activity.

The CPK elevations seen after catheterization reflect release of enzyme from noncardiac sources rather than from injured myocardium, Dr. Ludbrook said. Increased serum MB CPK isoenzyme activity, he added, remains a specific and sensitive criterion of myocardial damage in patients undergoing cardiac catheterization and coronary arteriography.

Coauthors of the two reports included Drs. Burton B. Sobel and Edward S. Weiss; H. Dieter Ambrose; and Elaine M. Carlson.



Survey Finds Little Change In Clinician Use of Rauwolfia

Continued from page 1

very muddy at the moment and I think it's going to take a lot of careful prospective looking-at with years of therapy."

"Breast cancer is very common in obese people and hypertension is very common in obese people. And hypertension is very common in the age group that gets breast cancer, around menopause. I think the only answers will come from prospective studies."

Dr. Jeremiah Stamler of Northwestern University Medical School calls the situation "troublesome." "There is reason for concern," he said, "but I think at this point the issue is open."

"Situation Troublesome" "I don't think one can conclude that a definite association [between rauwolfia use and cancer] has been demonstrated, or that a definite association has been refuted."

"I think the situation is troublesome because reserpine is a very useful drug. It's effective, and low in cost, and many people have tremendous risks because of hypertension."

"Pending further evaluation, we're continuing to use the drug. We're watching closely, but we're continuing to use it," Dr. Stamler said.

Dr. Herbert G. Langford, Director of the Division of Endocrinology at the University of Mississippi and chairman of the steering committee of the National Hypertension Detection and Followup Program, also said he feels more studies need to be done. On the basis of the studies so far, though, he said he would "bet against" a causal

Chronology of 3 Studies on Rauwolfia Therapy

The first studies to link rauwolfia therapy and breast cancer were done by interlocking groups at the Boston Collaborative Drug Surveillance Program, Oxford University, and the University of Helsinki (*Lancet*, Sept. 21, 1974.)

The next study, from the Chicago Peoples Gas Company (MT, December 25, 1974), found no evidence of a link between rauwolfia therapy—in men—and cancer, but indicated that there may be an association between hypertension and cancer.

Most recently, (MT, April 9), a Mayo Clinic study, using women with cholelithiasis as controls, found no excess of breast cancer in women who had been on rauwolfia therapy.

An H.E.W. ad hoc committee, meeting to assess these data at the National Heart and Lung Institute on March 24-25, called for more data and further examination.

relationship between reserpine and cancer.

What the whole matter suggests to him, Dr. Langford said, "is a cluster, or a constellation . . . or a syndrome, you might say, of being a little hypertensive, and a little obese, and going to the doctor, and getting drugs—and these could also go along with gallbladder disease."

He added that all his patients have been informed about the studies concerning rauwolfia derivatives and "practically none of them have asked to be taken off it."

One Man...and Medicine

ARTHUR M. SACKLER, M.D.,
International Publisher, Medical Tribune



Mystification

Part I

FOR YEARS, as we sought to quantitate experimental stress utilizing simple stimuli such as sound and vibration, we noted marked physiologic deviations in our experimental animals. I therefore was upset to confront Lennard *et al*'s pejorative "mystification" as a challenge to practicing physicians who use pharmacotherapy for relief of anxious and disturbed patients for what Lennard calls "common, everyday stresses of living." I first came across this neologism in their article published in 1970.¹ I did not realize then, as the authors cited, "The concept of 'mystification' [had] originally [been] described by Marx." It added to my mystification to observe that this introduction of Marxist terminology coexisted with the radical right, politically-motivated drug hysteria which was linking young drug abusers with the radical left.

Because I believe that the presumption of innocence and of good faith must extend to those with whom I disagree as well as those who think as I do, I put the matter aside. The pressure of events conspired to delay careful study of the claims of Lennard *et al*. In the past, in respect to most physicians and scientists, despite conflicting differences in reported findings the premise of innocence and good faith has for the most part proved out. In fact, such disputed biologic differences became a primary point of departure of our laboratory investigations which we have grouped under the rubric, "Common Unrecognized Variables in Biologic Experimentation."

Equate Physicians with "Pushers"?

Recently, I reread Lennard *et al*'s book, *Mystification and Drug Misuse*,² and reviewed their 1970 and 1967 articles.³ I would have hoped that these authors also started with a presumption of innocence and the premise of good faith for their fellow professionals. It serves the interest of neither science nor society, neither of patient nor physicians to write, as they do, that "The administration of a drug serves latent functions for physicians as well as for patients and for pushers as well as addicts."

To equate physicians subtly, or not so subtly, with pushers, patients with addicts, does not contribute to physician-patient collaboration. I must confess I am mystified as to the motivations which lead Lennard *et al* to suggest that major rationale for a doctor's prescription is that it "legitimizes the doctor-patient contract," may help "a physician to maintain a sense of accomplishment and to allay his frustration" and "may help some physicians retain a sense of mastery in the doctor-patient relationship." When, as an intern, house physician, and resident, I gave sedatives on evening rounds, I wasn't (as the authors imply) eliminating the "inconvenience of having to respond to demands from patients." I

believed I was promoting a good night's sleep, in a difficult environment, under trying circumstances.

Belief about Drugs

The book advances the authors' belief that "The contemporary trend of increasing prescriptions of psychoactive drugs seems to be contributing to the recruitment of more and more persons into a way of life in which the regulation of personal and interpersonal processes is accomplished through the ingestion of drugs."

There is no consistency, however, between the known pattern of illegal psychoactive drug abuse—highest in young males, and for hard drugs, highest in black males, and the authors' report that a national survey of prescription drug use in 1967 "found that twice as many women (31 per cent) as men (15 per cent) had used psychoactive agents during the preceding 12 month period. . . . There were also major differences in psychoactive drug use among religious and racial groups. The same survey found that Jews use psychoactive drugs considerably more than do Catholics or Protestants and that the percentage of Negroes using psychoactive drugs is only about one-half (13 per cent) that of whites (26 per cent)." Clearly there is no relationship either between the number of physicians practicing or prescribing in ghetto areas and heroin abuse; nor is the frequency of alcoholism higher in Jews than in Catholics or Protestants; nor does the incidence of alcoholism relate to the sex differences in psychoactive prescriptions. In fact, these are 180 degrees out of phase.

Addiction and Social Influence

Despite the indisputable fact that social influences do affect addiction, it must be recognized that the most frequent and most serious prototype of Western addiction, alcoholism, not only cuts across economic groups in any one society but affects even the most varied societal structures. Alcoholism in capitalist Atlantic City does not distinguish itself readily from alcoholism in communist Zagreb; Leningrad does not have a lower incidence than London, or Warsaw than Washington. As to non-western psychotropics, the use of charas in Calcutta doesn't differ in ultimate effects from marijuana in Marrakesh, ganga in Ghana, kif in Kashmir, or hashish in tribal areas of Africa.

Which social system has solved the

problem of psychoactive drug abuse? Apparently neither the tribal nor communist forms of society, nor the democratic, nor nonarchival systems. It becomes imperative, therefore, to seek to isolate relevant elements with realistic potentials for prevention or control or reduction in abuse.

Next week "mystification" continues, Part II.

1. Science, 169:438, July 31, 1970.
2. Mystification and Drug Misuse, H. L. Lennard *et al*, Jossey-Bass, Inc., San Francisco, 1971.
3. J. Nerv. & Ment. Dis 145:69, July, 1967.

EPICRAMS—Clinical and Otherwise

A sick man dreams nothing so dreadful that some philosopher isn't saying it.

Marcus Terentius Varro
116-27 B.C.
Satires, frag. 122

Medicine on Stamps

Jabir



Born in 705, Jabir, or Geber, was a healer, though he is best known as the father of modern chemistry. He is credited with the discovery of nitric acid and aqua regia and described distillation, filtration, and sublimation. About 500 books have been attributed to his authorship.

Text: Dr. Joseph Kler
Stamp: Minkus Publications, Inc., New York

Doctor Resistance to PSROs Is Dying Out, Says Simmons

Continued from page 1

changed their positions—for example, Indiana, Illinois, Nebraska. I'm convinced that in virtually every area of the country, the profession will come forward and do the job, and there'll be no need to bring in non-physicians to organize the programs."

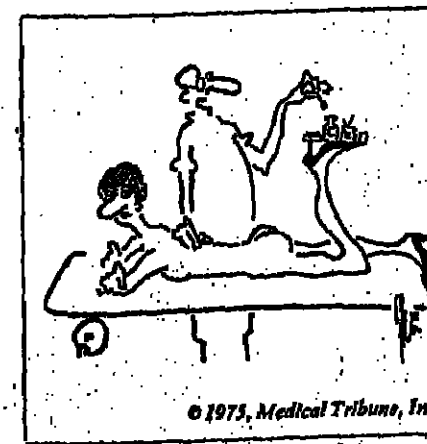
According to Dr. Simmons, there are only four states (Georgia, Texas, Oklahoma and Louisiana) where no plans have yet been filed. The PSRO mandate of the 1972 Social Security amendments, designed to oversee hospital care of Medicaid and Medicare patients, carries a Jan. 1, 1976 deadline for submission by local physicians of acceptable plans of implementation to H.E.W. Failing this, medical schools or consumer groups might be brought in to tailor the program in place of physicians.

Measuring Up to Expectations

Early data on operative PSROs indicates to Dr. Simmons that they are measuring up to expectations. He cited reports of decreased length of hospital stays from each of the districts. Less tangibly, he believes there has been "an improvement in the quality of care provided" in these districts. He revealed that several private insurers, among them the "Blues" and the Health Insurance Association of America, have expressed interest in having PSRO committees pass on their patients, and are now negotiating with H.E.W. to coordinate and unify review mechanisms.

"Eventually, I expect there will be a uniform system of reviewing all hospital patients, whether their bills are being picked up by the government or third-party private insurers, and irrespective of when or whether we get National Health Insurance. I don't rule out the possibility that one-day outpatients will be covered, too. Some PSROs are already trying this experimentally."

Although he thinks PSRO will mesh smoothly with a National Health Insurance scheme, Dr. Simmons does not see NHJ as a prerequisite to success.



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Harvard Enters Pact on Cancer With Monsanto

Medical Tribune Report

BOSTON—The Harvard Medical School and the Monsanto Company are understood to have entered into a "working arrangement" under which the company will provide cancer research financing in return for the commercial rights to any resulting discoveries.

The funding, over 12 years, may reach a total of \$23,000,000, plus biologic materials, equipment development, and industrial know-how, according to informed sources. The money is intended to support the work of two Harvard scientists, Drs. M. Judah Folkman and Bert L. Vallee, who have each made important discoveries in basic cancer research.

The school and the company described the arrangement as an alliance designed to permit the Harvard scientists to pursue their research wherever it may lead, without interference.

An independent advisory board will protect the rights of both parties and those of the public, it was reported.

Toward Rapid Application

Framers of the agreement not only see mutual benefits, but also feel there is a need to develop a system of applying accumulating knowledge more rapidly to meet human needs. They expect this alliance to generate practical techniques for accomplishing this.

Dr. Folkman is chief of surgery at the Children's Hospital Medical Center here. He is best known perhaps for his work in growing whole malignant tumors to permit long-term studies on their growth rate and metabolism. He recently identified a tumor angiogenesis factor (TAF) that triggers the development of the blood vessels that feed such tumors.

Dr. Vallee's research has focused on the function of a zinc-dependent enzyme in the leukemic process that he hypothesized more than 25 years ago, long before tools for quantitating it existed. He is director of the medical school's Biophysics Research Laboratory at the Peter Bent Brigham hospital.

In the Harvard-Monsanto project, the two scientists will join forces in a greatly expanded effort to determine the nature and function of TAF in order to modify its action.

Monsanto's capabilities for synthesizing and concentrating chemical compounds are expected to be important contributions to the Vallee-Folkman research.

Herbert A. Shaw, a spokesman for the medical school, said that Harvard has never entered into such a relationship before. If it succeeds, it may provide a solution to the recent drastic cutbacks in support from traditional research sources.

Rural Service Required

Medical Tribune World Service

CARACAS—All Venezuelan medical school graduates will be required to spend one year working in small rural towns before being permitted to practice in the cities, under measures now being drafted by the Government.

"It should be emphasized...that most patients tolerate guanethidine with minimal side effects, when dosage adjustment is carefully managed."

Freis ED: The Modern Management of Hypertension. US Government Printing Office, 1973, pp 13-14.

when hypertension threatens to outrun control...

"It should be emphasized...that most patients tolerate guanethidine with minimal side effects, when dosage adjustment is carefully managed."

Often, some of the side effects associated with such drugs as the ganglionic blockers can be avoided by substituting a little Ismelin in the treatment of moderate hypertension.

Because guanethidine is perhaps the most effective antihypertensive agent ever available, Ismelin usually brings blood pressure down to stay. And Ismelin produces no parasympatholytic effects.² Further, when used with thiazides, the required addition may be low.³

Of course, whenever Ismelin is added to other antihypertensives, initial doses should be small, and increased gradually by small increments.

Once blood pressure control is achieved, all drug dosages should be reduced to lowest effective level, often minimizing side effects.

Patients should be warned about the potential hazards of orthostatic hypotension, and cautioned to avoid sudden or prolonged standing or exercise.

A little extra patient cooperation may be required.

But may well be worth it—for the extra protection Ismelin offers against the dangers of uncontrolled hypertension.

References:

1. Freis ED: The Modern Management of Hypertension. US Government Printing Office, 1973, pp 13-14.
2. Freis AN: Hypertension. In: Conn AF (ed): Current Therapy. Philadelphia, WB Saunders Co, 1974, p 204.
3. Gilford RW Jr: Drugs for arterial hypertension. In: Modell W (ed): Drugs of Choice, 1973, 12th ed. St. Louis, The CV Mosby Co, 1973, pp 390-395.

Ismelin® sulfate

(guanethidine sulfate)

INDICATIONS: Moderate and severe hypertension either alone or as an adjunct.

CONTRAINDICATIONS: Known or suspected pheochromocytoma; hypersensitivity; frank congestive heart failure not due to hypertension; patients taking MAO inhibitors.

WARNINGS: Ismelin is a potent drug and can lead to disturbing and serious clinical problems. Physicians should be familiar with the details of its use before prescribing, and patients should be warned not to deviate from instructions.

Warn patients about the potential hazard of orthostatic hypotension, which can occur frequently and is most marked in the morning and is accentuated by hot weather, alcohol, or exercise. To help prevent fainting, warn patients to sit or lie down with onset of dizziness or weakness, which may be particularly bothersome during the initial period of dosage adjustment and with postural changes. The potential occurrence of these symptoms may require alteration of previous daily activity. Caution patients to avoid sudden or prolonged standing or exercise while taking the drug.

add a little **Ismelin** sulfate
(guanethidine sulfate)
...because the goal is 140/90

Concurrent use with rauwolfia derivatives may cause excessive postural hypotension, bradycardia, and mental depression.

If possible, withdraw therapy 2 weeks prior to surgery to reduce the possibility of vascular collapse and cardiac arrest during anesthesia. If emergency surgery is indicated, administer pressor and anesthetic agents cautiously in reduced dosage and have oxygen, atropine, vasopressors, and IV solutions ready for immediate use to treat vascular collapse. Vasopressors should be used with extreme caution in patients on Ismelin because of the possibility of exaggerated response and the greater propensity for cardiac arrhythmias.

Dosage requirements may be reduced in presence of fever. Exercise special care when treating patients with a history of bronchial asthma, since their condition may be aggravated.

Usage in Pregnancy
The safety of Ismelin for use in pregnancy has not been established; therefore, this drug should be used in pregnant patients only when, in the judgment of the physician, its use is deemed essential to the welfare of the patient.

PRECAUTIONS: The effects of guanethidine are cumulative over long periods; initial dose should be small and increased gradually in small increments. Use very cautiously in hypertensives with renal disease and nitrogen retention or rising BUN levels; coronary disease with angina.

clency or recent myocardial infarction; cerebral vascular disease, especially with encephalopathy. Do not give Ismelin to patients with severe cardiac failure except with extreme caution.

In incipient cardiac decompensation weight gain or edema may be averted by the administration of a thiazide. Remember that both digitalis and Ismelin slow the heart rate.

Peptic ulcers or other chronic disorders may be aggravated by a relative increase in parasympathetic tone.

Amphetamine-like compounds, stimulants (eg, epinephrine, methylphenidate), tricyclic antidepressants (eg, amitriptyline, imipramine, desipramine), and other psychopharmacologic agents (eg, phenothiazines and related compounds), and oral contraceptives may reduce the hypotensive effect of guanethidine. Discontinue MAO inhibitors for at least one week before starting Ismelin.

ADVERSE REACTIONS: Frequent reactions due to sympathetic blockade—dizziness, weakness, lightheadedness, syncope. Frequent reactions due to unopposed parasympathetic activity—bradycardia, increase in bowel movements, diarrhea (may be severe and necessitate discontinuance of the drug). Other common reactions—inhibition of ejaculation, fluid retention, edema, congestive heart failure, drowsiness, fatigue, nausea, vomiting, nocturia, urinary incontinence, dermatitis, scalp hair loss, dry mouth, rise in BUN, pigmentation of the skin, blue-

ring of vision, parotid tenderness, myalgia, muscle tremor, mental depression, chest pain (anginal), chest parasthesias, nasal congestion, weight gain, and asthma in susceptible individuals. Although a causal relationship has not been established, a few instances of anemia, thrombocytopenia and leukopenia have been reported.

DOSEAGE AND ADMINISTRATION: Initial dosage should be low and increased gradually by small increments.

Before starting therapy, consult complete product literature.

HOW SUPPLIED: Tablets, 10 mg (pale yellow, scored) and 25 mg (white, scored); bottles of 100 and 1000.

CIBA Pharmaceutical Company
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Tribune Economic Analysis



Stocks Running Collision Course With Bond Trend

The bond market always determines not only the direction of stock market moves but also the timing. A recent bond report in the *Wall Street Journal* took the form of an interview with the chief credit rater at Standard and Poor's. It quoted him as warning that business generally—and top-rated ones in particular—are underfinanced. It cites him as predicting a still more desperately underfinanced condition for the U.S. Government; he guesstimated that it needs to raise at least \$90 billion this year in the public market.

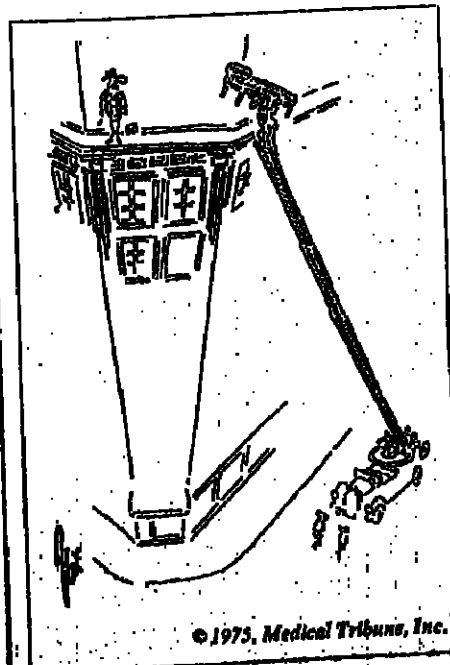
"That will leave precious little for everybody else," the *Wall Street Journal* quotes the Standard and Poor's rater as saying. There's no way the Federal Government can play the heavy as the big pig at the credit trough and still leave enough for the smaller credit users who are its partners in tax collections.

On Borrowed Time

But the buildup in new demand for bond money and the run-up stock prices are on a collision course. The run-up in stock prices may reverse itself. The buildup in the demand for new bond money is not about to. The trustworthy time for a run-up in stock prices is when no one wants to raise new money. When everyone who can get it needs it, like now, stock prices become suspect. They never run uphill against bond yields for very long.

The stock market is living on borrowed time that is running out in the face of a bond market being broken by Treasury borrowings.

The runaway in Government borrowings, plus the underfinanced conditions of the best corporations, guarantees that bond yields will remain at 9 per cent or go still higher. The reversal in stock prices may prove more serious than a mere correction.



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C I B A

Group B Strep Infections 'a Major Threat' to Newborn

Medical Tribune Report

NEW YORK—Group B hemolytic streptococcal infections have become a major threat to newborn infants throughout the U.S., Dr. Martha D. Yow, Professor of Pediatrics, Baylor College of Medicine, told a National Foundation symposium on fetal and neonatal infections here.

The infantile diseases caused by Group B streptococci, "relatively insignificant" ten years ago, have not replaced others in the nursery, Dr. Yow said, but have been added on. For example, the incidence of bacterial meningitis in the newborn at five hospitals in Houston, Texas, which "parallels experience in other cities," has virtually doubled during the last five years, while incidence of infections from other groups of streptococci has not appreciably diminished.

Broad Spectrum of Illness

The spectrum of illnesses caused by Group B streptococci, she said, ranges from asymptomatic colonization to serious and fatal disease, and includes septicemia, meningitis, arthritis, pneumonia, empyema, osteomyelitis, endocarditis, cellulitis and conjunctivitis.

When onset occurs during the first week of life, there is a high mortality rate (60-75 per cent), severe multi-system involvement, and the etiologic agent may be any of five serotypes of streptococci; when onset is after the first week mortality is lower (14-18 per cent), infection is due almost exclusively to type III organisms, and the affected site is mainly the meninges.

According to Dr. Yow, the mode of transmission of infection in the "early onset syndrome" is directly from the mother to the infant; this has been determined by the "complete concordance between the strain of organism harbored in the mother's vagina and the organism her infant was colonized by." The acquisition of infection in "late onset disease" is less clear, but there are suggestive signs that the nursery environment itself is an important source of colonization. A Houston study last year found that the rate of infant colonization by Group B streptococci from just after birth to time of discharge from hospital rose from 22 to 65 per cent.

Discrepancy With Attack Rate

The same study noted a marked discrepancy between the high infant colonization rate (65 per cent) and the disease attack rate in the infants which was only three per thousand live births (.3 per cent). Dr. Yow stated that there was little known as yet concerning the immune mechanisms that might account for this, but it is recognized that low birth weight and prolonged rupture of maternal membranes do predispose to invasion in "early onset" disease.

Maternal infection with group B streptococci is generally inapparent or expressed as bacteremia or amnionitis with low grade perinatal fever. Bacteriologic isolation and diagnosis are accomplished by growing pure colonies of the infecting organism, extracting the group carbohydrates, and demonstrat-

ing a serological reaction between the extracted antigen and specific grouping antiserum.

Alternative Method Suggested

Since this procedure may be impractical in the ordinary clinical laboratory, Dr. Yow suggested an alternative method of establishing streptococcal grouping using a battery of five tests: determination of hemolytic activity, bacitracin susceptibility, hydrolysis of sodium hippurate, hydrolysis of esculin in presence of 40 per cent bile, and tolerance to 6.5 per cent NaCl broth.

Where serotyping is required, it can be requested from the Center for Disease Control, where a rapid fluorescent antibody technique for identifying

group B streptococci has also recently been developed.

Whatever strain of B-streptococcus is discovered as the etiologic agent, immediate and vigorous treatment with penicillin is "essential because of the serious and fulminant nature of these illnesses, both in the early- or late-onset syndromes," Dr. Yow said. Penicillin administered intravenously over a period of ten days will eradicate most of the organisms from the blood, spinal fluid, and other foci, she said, although tissue damage may be irreparable and the throat and rectum may continue to harbor the organism.

Besides vigilant cleanliness and scrupulous hand-washing on the part of nursery personnel, there were no

prophylactic or preventive measures against infant B-streptococcal disease that Dr. Yow could recommend at present.

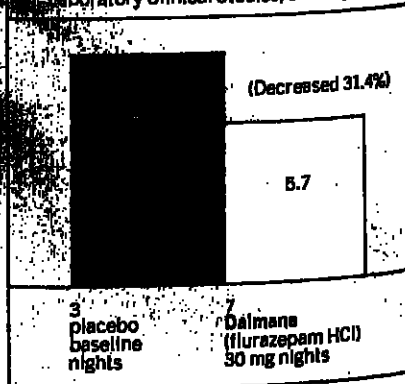
Routine treatment of vaginally colonized pregnant females with penicillin could not be justified, in view of the widespread prevalence of colonization and antibiotic side-effects, she said. "You would have to treat 500 adults per 1,000 live births for a disease whose attack rate is no more than three in a thousand," Dr. Yow pointed out, "and even then, we know that late-onset disease can be acquired nosocomially."

Instead she called for more investigation into the factors that influence the ecology of the maternal vagina, changes in herd immunity, virulence as related to serotype, and the natural history of the carrier state. E.G.

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Average Number of Nighttime Awakenings¹⁻⁴ for Geographically Separated Sleep Research Laboratory Clinical Studies, 16 Subjects



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1. Karacan I, Williams RL, Smith JR: The sleep laboratory in the investigation of sleep and sleep disturbances. Scientific exhibit at the 124th annual meeting of the American Psychiatric Association, Washington DC, May 3-7, 1971
2. Frost JD Jr: A system for automatically analyzing sleep. Scientific exhibit at the 24th annual Clinical Convention of the American Medical Association, Boston, Nov 29-Dec 2, 1970; and at the 42nd annual scientific meeting of the Aerospace Medical Association, Houston, Apr 26-29, 1971
3. Vogel GW: Data on file, Medical Department, Hoffmann-La Roche Inc., Nutley NJ
4. Dement WC: Data on file, Medical Department, Hoffmann-La Roche Inc., Nutley NJ
5. Data on file, Medical Department, Hoffmann-La Roche Inc., Nutley NJ

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Indications: Effective in all types of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings and/or early morning awakening; in patients with recurring insomnia or poor sleeping habits; and in acute or chronic medical situations requiring restful sleep. Since insomnia is often transient and intermittent, prolonged administration is generally not necessary or recommended.

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(flurazepam HCl)

One 30-mg capsule h.s.—usual adult dosage (15 mg may suffice in some patients).
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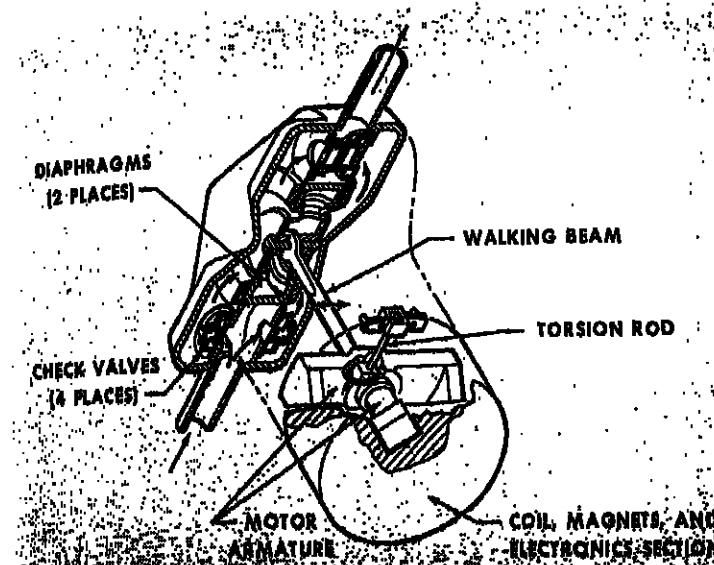
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- sleep within 17 minutes, on average
- sleep for 7 to 8 hours, on average, with a single h.s. dose.

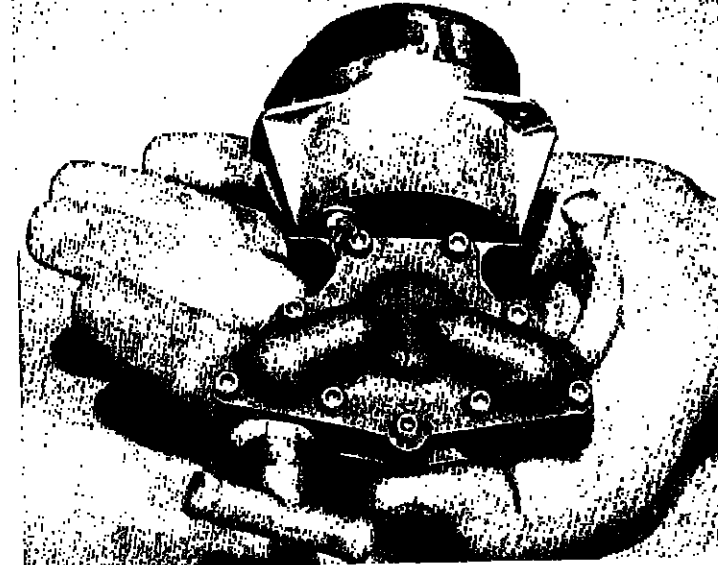


ROCHE LABORATORIES
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

NASA Pump Adaptable to Heart-Lung Systems Disrupts Fewer Red Blood Cells



In the Apollo pump two Dacron diaphragms, coated with butyl rubber, are attached at the end of an oscillating beam mounted on a torsion bar. Each diaphragm covers a chamber equipped with inlet and outlet check valves. While one diaphragm is pressurizing its chamber, thereby opening its outlet valve, the other diaphragm is providing suction to the alternate chamber opening its inlet valve. When the oscillating beam moves in the opposite direction, each chamber reverses its function.



BOSTON—A pump originally designed to circulate fluids in astronauts' space suits is being tested for use in extra-corporeal heart-lung systems and "could conceivably" make it possible for the heart to be bypassed for an indefinite number of days or weeks, a team of scientists reported at a meeting of the Association for the Advancement of Medical Instrumentation.

The Apollo double diaphragm pump (ADDP), which is also being investigated for adaptation in implantable artificial heart-lung systems, is significantly less destructive to red blood cells than any existing pump now used in heart-lung machines, the team reported. These findings were based on

Continued on page 23

Doctors Are Alerted To Tick Typhus Rise

Medical Tribune Report

NEW ORLEANS—With the approach of the late spring and summer outdoor season, physicians should suspect tick typhus, or Rocky Mountain spotted fever, when confronted with an acute febrile exanthematous illness—especially in a woman or child, the Pediatric Pathology Club was told here.

An unprecedented 774 cases of the disease were reported last year by the Public Health Service, 416 of them in the South Atlantic states where tick typhus is endemic, according to Dr. Hal K. Hawkins of Duke University School of Medicine. In 1973 the national total was 638 cases, the previous record.

Dr. Hawkins, a pathologist, warned that the typhus may be mistaken for measles and meningococcemia.

He reported to the Club on experience with 120 children who were treated at Duke over the last 30 years. All had the clinical hallmarks: fever, rash, and a history of tick bite.

Hyponatremia was present in 43 of 49 children tested, reflecting the increased vascular permeability characteristics of the disease. Thrombocytopenia was present in 25 of 33 patients in whom quantitative platelet counts were made. Findings at autopsy reflected generalized vasculitis.

Dr. W. D. Bradford is in charge of the Duke study. Dr. C. R. Abramowsky and Dr. Hawkins are his associates.

MBD Case History #1

1971...a difficult child, a distraught mother

Medical diagnosis: MBD.



Robert Boynton,* second of five children, born October 7, 1963. Normal pregnancy and delivery.¹

From the age of 3, Robert's mother found him "hard to handle," "wilder" than his brothers and sisters.¹

At age 6, after an "extremely difficult" experience in kindergarten, Robert was referred to a pediatric neurologist. The examination and later psychological testing revealed a host of the neurologic "soft signs," plus an abnormal EEG.¹

The diagnosis: average intelligence, but multiple signs of an underlying organic dysfunction.¹

At age 7, Robert was placed in a special first-grade class called an "extended readiness program."¹

Later that year, her child's continued problems at school and at home made Robert's mother "increasingly desperate" for help.

1974...a regular fourth-grader, accepted at home

In the opinion of the physician, methylphenidate (Ritalin) was called for to help the child over the obstacles of hyperactivity. So he initiated a trial of the drug, which was then implemented on school days only.¹

The improvement in classroom performance and behavior was "prompt and dramatic." Robert's teacher could "scarcely believe" that he was the same child.¹

For the past 4 years (as of April 1974), Robert has been maintained on 15 mg methylphenidate daily during school periods. During the summer he attends day camp and is not on medication. He is in a regular fourth-grade class, and behavioral problems at home have lessened. Robert's parents now find it much easier to accept their son.¹

*Note: In this presentation, clinical material has been used factually with the permission of the physician. However, identities have been concealed and names changed.

How other children with MBD

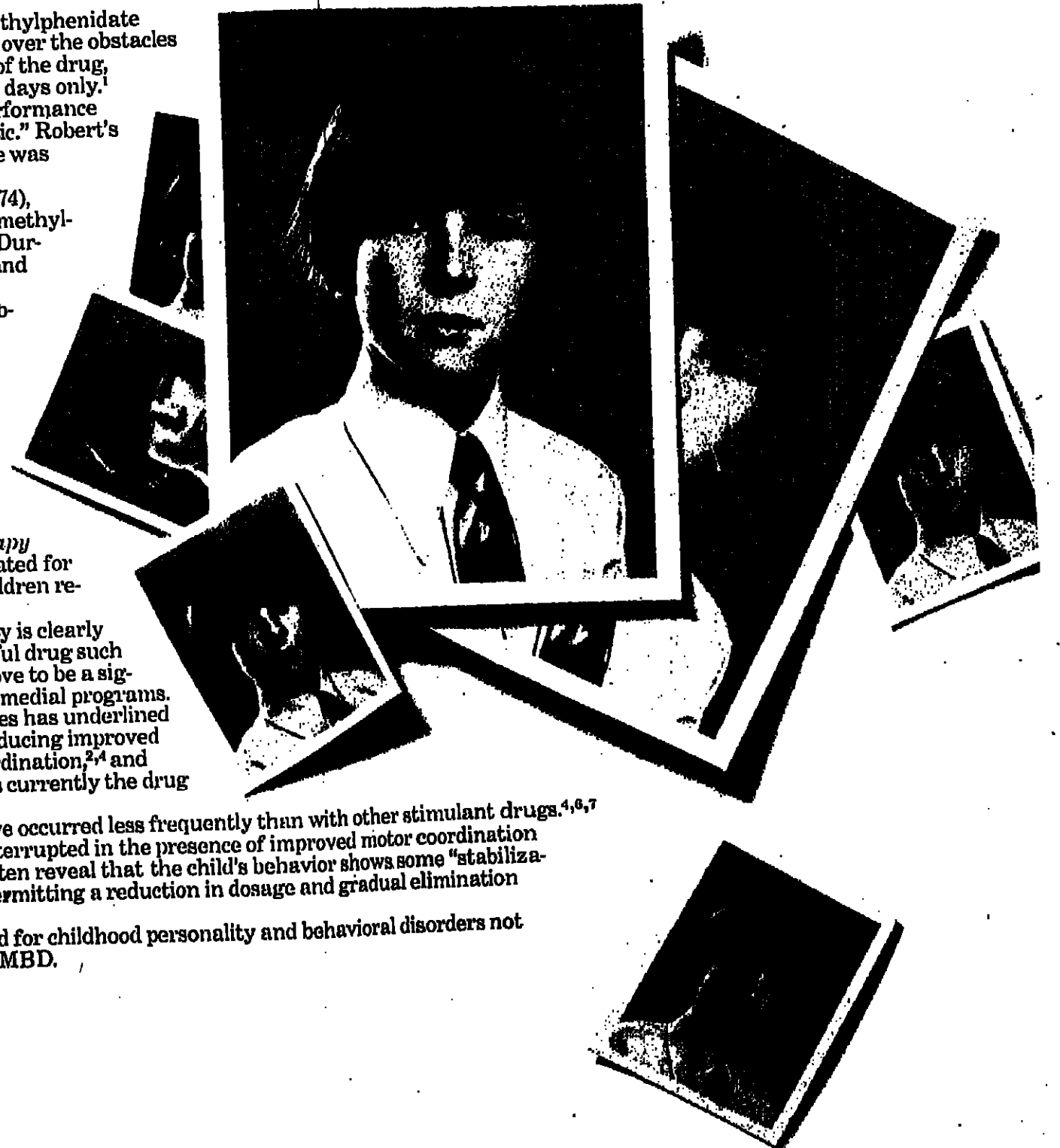
can benefit from methylphenidate therapy
Of course, medication is not indicated for all MBD children; nor will all such children respond to drug therapy.

However, when pharmacotherapy is clearly indicated, the use of a widely successful drug such as Ritalin (methylphenidate) may prove to be a significant element in many complete remedial programs.

Over a decade of controlled studies has underlined the beneficial effects of Ritalin in producing improved behavior ratings,^{2,3} better motor coordination^{2,4} and cognition and learning.^{2,4} Indeed, it is currently the drug of choice in many MBD situations.⁵

And side effects with Ritalin have occurred less frequently than with other stimulant drugs.^{4,6,7} Dosage should be periodically interrupted in the presence of improved motor coordination and behavior. These interruptions often reveal that the child's behavior shows some "stabilization" even without chemotherapy, permitting a reduction in dosage and gradual elimination of drug therapy.

Of course, Ritalin is not indicated for childhood personality and behavioral disorders not associated with medical diagnosis of MBD.



An MBD child on the road to maturity

Ritalin® hydrochloride C (methylphenidate hydrochloride)

TABLETS
Minimal Brain Dysfunction in Children—as adjunctive therapy to other remedial measures (psychological, educational, social).
Special Diagnostic Considerations: Specific etiology of Minimal Brain Dysfunction (MBD) is unknown, and there is no single diagnostic test. Adequate diagnosis requires the use not only of medical but of social psychological, educational, and social resources.
Characteristics commonly reported include: chronic history of short attention span, distractibility, emotional lability, impulsivity, and moderate to severe hyperactivity; minor neurological signs and abnormal EEG. Learning may or may not be impaired. The diagnosis of MBD must be based upon a complete history and evaluation of the child and not solely on the presence of one or more of these characteristics. Drug treatment is not indicated for all children

with MBD. Stimulants are not intended for use in the child who exhibits symptoms secondary to environmental factors and/or primary psychiatric disorders, including psychosis. Appropriate educational placement is essential and psycho-social intervention is generally necessary. When remedial measures alone are insufficient, the decision to prescribe stimulant medication will depend upon the physician's assessment of the chronicity and severity of the child's symptoms.
CONTRAINDICATIONS
Marked anxiety, tension, and agitation; since Ritalin may exacerbate these symptoms. Also contraindicated in patients known to be hypersensitive to the drug and in patients with glaucoma.

WARNINGS
Ritalin should not be used in children under six years, since safety and efficacy in this age group have not been established.
Sufficient data on safety and efficacy of long-term use of Ritalin in children with minimal brain dysfunction are not yet available. Although a causal relationship has not been established, height has been reported with long-term use of stimulants in children. Therefore, children requiring long-term therapy should be carefully monitored.
Ritalin should not be used for severe depression or for the prevention of normal fatigue states.
Ritalin may lower the convulsive threshold in patients with or without prior seizures, with or without prior EEG abnormalities, even in alcohol convulsants and Ritalin should be discontinued if seizures occur. Ritalin should be discontinued, use cautiously in patients with hypertension. Blood pressure should be monitored at appropriate intervals in all patients taking Ritalin, especially those with hypertension.

Drug Interactions
Ritalin may decrease the hypotensive effect of guanethidine. Use cautiously with pressor agents and MAO inhibitors. Ritalin may inhibit the metabolism of coumarin anticoagulants, anticonvulsants (phenobarbital, diphenylhydantoin, primidone), phenylbutazone, and tricyclic antidepressants (imipramine, desipramine). Downward dosage adjustments of these drugs may be required when given concomitantly with Ritalin.
Usage in Pregnancy
Adequate animal reproduction studies to establish safe use of Ritalin during pregnancy have not been conducted. Therefore, until more information is available, Ritalin should not be prescribed for women of childbearing age unless, in the opinion of the physician, the potential benefits outweigh the possible risks.

Ritalin® (methylphenidate)

can help when medication is indicated

Drug Dependence
Ritalin should be given cautiously to emotionally unstable patients, such as those with a history of drug dependence or alcoholism, because such patients may increase dosage on their own initiative.
Chronic abuse use can lead to marked tolerance and psychic dependence with varying degrees of abnormal behavior.
Abrupt discontinuation of Ritalin may result in psychotic episodes can occur, especially with parental abuse. Careful supervision is required during drug withdrawal, since severe depression as well as the marked, long-term follow-up may be required because of the patient's basic personality disturbances.

PRECAUTIONS
Patients with an element of agitation may react adversely to discontinuation therapy if necessary. Periodic CBC, differential, and platelet counts are advised during prolonged therapy.

ADVERSE REACTIONS
Nervousness and insomnia are the most common adverse reactions but are usually controlled by reducing dosage and omitting the drug in the afternoon or evening. Other reactions include: hypersensitivity (including skin rash, urticaria, fever, arthralgia, exfoliative dermatitis, erythema multiforme with histoplasma-like lesions, blood necrotizing vasculitis, and thrombocytopenic purpura); anorexia; nausea; dizziness; palpitations; headache; dyskinetic dyskinesias; blood pressure and pulse changes, both up and down; tachycardia; angina; cardiac arrhythmia; abdominal pain; weight loss during prolonged therapy. Toxic psychosis has been reported. Although a definite causal relationship has not been established, the following have been reported in patients taking this drug: leukopenia and/or anemia; a few instances of scalp hair loss.
In children, loss of appetite, abdominal pain, weight loss during prolonged therapy, insomnia, and tachycardia may occur more frequently; however, any of the other adverse reactions listed above may also occur.

DOSEAGE AND ADMINISTRATION
Children with Minimal Brain Dysfunction (6 years and over)
Start with small doses (eg, 5 mg before breakfast and lunch) with gradual increments of 5 to 10 mg weekly. Daily dosage above 60 mg is not recommended. If improvement is not observed after appropriate dosage adjustment over a one-month period, the drug should be discontinued. If paradoxical aggravation of symptoms or other adverse effects occur, reduce dosage, or, if necessary, discontinue the drug.
Ritalin should be periodically discontinued to assess the child's condition. Improvement may be sustained when the drug is either temporarily or permanently discontinued.
Drug treatment should not be discontinued after initiation and usually may be discontinued after puberty.
HOW SUPPLIED
Tablets, 5 mg (pale yellow), bottles of 100, 500, and 1000.
Tablets, 20 mg (pale green, scored), bottles of 100, 500, 1000, and Accu-Pak blister units of 100, 500, and 1000.

Tablets, 5 mg (pale yellow); bottles of 100, 500, and 1000.
Consult complete product literature before prescribing.
Rev. 3/73
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C I B A

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Esidrix. It is still unsurpassed as a basic diuretic/anti-hypertensive. And many patients with edema rarely need a more potent diuretic.

Contraindications include anuria. Use cautiously in patients with impaired renal or hepatic function.

Esidrix® (hydrochlorothiazide)

for year-after-year control of mild hypertension



Esidrix® (hydrochlorothiazide)

INDICATIONS
Hypertension and edema.

CONTRAINDICATIONS
Anuria; hypersensitivity to this or other sulfonamide-derived drugs. The routine use of diuretics in otherwise healthy pregnant women with or without mild edema is contraindicated and possibly hazardous.

WARNINGS
Use with caution in severe renal disease. In patients with renal disease, thiazides may precipitate azotemia. Cumulative effects of the drug may develop in patients with impaired renal function. Thiazides should be used with caution in patients with impaired hepatic function or progressive liver disease, since minor alterations of fluid and electrolyte balance may precipitate hepatic coma. Thiazides may be additive or potentiative of the action of other antihypertensive drugs. Potentiation occurs with ganglionic or peripheral adrenergic blocking drugs.

Sensitivity reactions are more likely to occur in patients with a history of allergy or bronchial asthma. The possibility of exacerbation or activation of systemic lupus erythematosus has been reported.

Usage in Pregnancy
Usage of thiazides in women of childbearing age requires that the potential benefits of the drug be weighed against its possible hazards to the fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult.

Nursing Mothers
Thiazides cross the placental barrier and appear in cord blood and breast milk.

PRECAUTIONS
Periodic determination of serum electrolytes to detect possible electrolyte imbalance should be performed at appropriate intervals. Observe patients for clinical signs of fluid or electrolyte imbalance (hypotension, hypochloremic alkalosis, and hypokalemia). Serum and urine electrolyte determinations are particularly important when the patient is vomiting excessively or receiving parenteral fluids. Medication such as digitalis may also influence serum electrolytes. Warning signs are dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia, and gastrointestinal disturbances such as nausea or vomiting.

Hypokalemia may develop with thiazides as with any other potent diuretic, especially during brisk diuresis, when severe cirrhosis is present, or during concomitant administration of steroids or ACTH. Interference with adequate oral intake of electrolytes will also contribute to hypokalemia. Digitalis therapy may exaggerate metabolic effects of hypokalemia especially with reference to myocardial activity.

Any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver disease or renal disease). Dilutional hyponatremia may occur in edematous patients in hot weather; appropriate therapy is water restriction rather than administration of salt, except in rare instances when the hyponatremia is life-threatening. In actual salt depletion, appropriate replacement is the therapy of choice.

Transient elevations in plasma calcium may occur in patients receiving thiazides, particularly in those with hyperparathyroidism. Pathological changes in the parathyroid gland have been reported in a few patients on prolonged thiazide therapy.

Hyperuricemia may occur or frank gout may be precipitated in certain patients. Insulin requirements in diabetic patients may be increased, decreased, or unchanged. Latent diabetes may become manifest during thiazide administration.

Thiazide drugs may increase the responsiveness to tubocurarine. The antihypertensive effects of the drug may be enhanced in the post-sympathectomy patient. Thiazides may decrease arterial responsiveness to norepinephrine. This is not sufficient to preclude effectiveness of the pressor agent for therapeutic use.

If nitrogen retention indicates onset of progressive renal impairment, consider withholding or discontinuing diuretic therapy.

Thiazides may decrease serum PBI levels without signs of thyroid disturbance.

ADVERSE REACTIONS
Gastrointestinal—nausea, gastric irritation, nausea, vomiting, cramping, diarrhea, constipation, jaundice (intrahepatic cholestatic), pancreatitis, anorexia, flatulence, dyspepsia, vertigo, dizziness, headache, xanthopsia. Dermatologic—hypersensitivity—pruritus, photosensitivity, rash, urticaria, necrotizing angitis, Steven-Johnson syndrome, and other hypersensitivity reactions. Hematologic—leukopenia, agranulocytosis, thrombocytopenia, aplastic anemia. Cardiovascular—orthostatic hypotension may occur and may be potentiated by alcohol, barbiturates, or narcotics. Other—hyperglycemia, glycosuria, hyperuricemia, muscle aches, weakness, restlessness. Whenever adverse reactions are moderate or severe, reduce dosage or withdraw therapy.

DOSEAGE
Individualize dosage by titrating for maximum therapeutic response at the lowest possible dose.

Hypertension Initial—Usual dose 75 mg daily.

Maintenance—After a week dosage may be adjusted downward to as little as 25 mg or upward to as much as 100 mg daily. Combined therapy—When necessary, other antihypertensives may be added gradually and with caution because of the potentiating effect of this drug. Dosages of ganglionic blockers should be halved.

Edema Initial—25 to 100 mg daily for several days.

Maintenance—25 to 100 mg daily or intermittently. Refractory patients may require up to 200 mg daily.

SUPPLIED
Tablets, 50 mg (yellow, scored); bottles of 30, 60, 100, 1000, 5000 and Aqua-pak blister units of 100.

Tablets, 25 mg (pink, scored); bottles of 100, 1000 and 5000.

Consult complete literature before prescribing.

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C I B A

TRIBUNE SPORTS REPORT

Proper Shoe Fit Important For Avoiding Ankle Injuries

Medical Tribune Report

SAN FRANCISCO—To help avert ankle injuries, team physicians should always check football players' shoes for proper fit, Dr. E. R. Guise of Detroit told the American Orthopaedic Society for Sports Medicine here.

Shoe soles that are too small predispose the foot to pronation or supination, he said.

Newer shoes with larger soles and cleats distributed near the edges of the soles should help cut down on the number of serious ankle injuries, Dr. Guise said, but physicians should still check for fit because football players "have a tendency to put a size 14 foot into a size 11 shoe."

Team's Injuries Studied

A study of the significant ankle injuries to members of a professional football team over a five-year period showed that 16 of 20 were pronation external rotation injuries and the rest were supination internal rotation injuries, he reported.

When minor as well as major ankle injuries were considered, the supination internal rotation injuries were found to be the more frequent.

Such injuries are usually treated with support and a supportive high-top shoe, Dr. Guise noted.

The pronation external rotation in-

juries, which kept players out of action from one and a half to seven weeks, typically occurred when a player making a sharp turn or cut either lost his balance or was tackled.

The sudden interruption in motion with the foot in an abnormal position, given the size and speed of football players, can place a force equal to 1,264 pounds of stress on the ankle, Dr. Guise explained.

While no correlation was noted between the type of playing surface and the type of ankle injury, he said, an uneven surface and a poor-fitting shoe were found to be contributing factors.

The more serious pronation injuries required rigid immobilization, usually in a cast for two weeks, followed by a period of supportive high-top shoes with exercise, compression, and whatever other treatment was indicated.

In pronation external rotation injuries, the anterior talofibular ligament is often ruptured, Dr. Guise said, and an extreme form of the injury is a fibular fracture.

If a pronation injury is suspected, plaster should be applied immediately to prevent pain and swelling, he advised. The temporary cast can be removed the next day, when a more thorough assessment is made and a new cast put on.



IMMATERIA MEDICA

Our Man Outside

Dr. Harold M. Childress of Jamestown, N.Y., has called our attention to a title on the recent program of the American Academy of Orthopedic Surgeons in San Francisco:

Hangman's Fracture—Long-Term Follow-up

Dr. Childress never saw a hanging, he says, but having once inspected the gallows in San Quentin he believes the follow-up would have to be extremely short. No so, said the authors—Dr. George C. Venters, H. Robert Brashcar, Edwin T. Preston, Daniel C. Vinson, all of Chapel Hill, N.C., who presented 30 cases. What they are talking about is a fracture through the neural arch of the second cervical vertebra with or without forward subluxation of the vertebral body of C-2 on the vertebral body of C-3. It seems you can get all this without being hanged, whether you deserve it or not.

Temple Fugit

In Britain commercial TV has banned Shirley Temple movies of the 1930s from children's programs. "Too mawkish and sentimental to interest today's children," 'twas said.

So far as we know the Shirley Temple movies were made for adults with mawkish and sentimental ideas about cute little children changing the grown-up world.

The kids knew better.

Typographical Infection

When a MEDICAL TRIBUNE writer referred to tonsillitis as a changed disease, Dr. J. E. Bowman of 18th Street, Washington, D.C., promptly asked if the change was that he spelled it with one "i".

Naturally, that wasn't the change, but it was a typographical infection that spread, it seems, from the writer to the proofreaders to the editors, who went home sick, sick, sick.

Clinical Cliche



The tissue was infiltrated.
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NASA Pump Disrupts Fewer Red Blood Cells

Continued from page 19

studies performed on the pump in its original form and "it is anticipated that modifications of the pump will provide further improvement in performance," they said.

The research is being conducted by Dr. Henry J. Heimlich, director of surgery, Jewish Hospital, Cincinnati; Mr. Neil Armstrong, former Apollo astronaut and now Professor of Aerospace Engineering at the University of Cincinnati; Dr. Edward A. Patrick, M.D., Ph.D., Professor of Electrical Engineering, Purdue University and Indiana University School of Medicine; and George Rieveschl, Jr., Ph.D., Sc.D., vice president for special projects at the University of Cincinnati.

Physiologic Problems

Existing heart-lung machines can be used safely only for several hours. "Several adverse physiologic effects occur in prolonged pumping of blood with a mechanical pump," the team explained. "These problems include hemolysis, 'ghosts' (envelopes left over after red blood cells disrupt), anemia, increased viscosity, protein denaturation (particularly albumin destruction), increased plasma turbidity, lipemia, and platelet abnormalities (especially thromboembolism and shortened survival of platelets)."

A pump that causes minimal destruction of blood elements and that possesses extended-use capabilities could help some patients survive an

acute coronary, post operative pneumonia, cardiac failure, pulmonary insufficiency, and other acute and chronic problems, the team indicated.

The Apollo double diaphragm pump "incorporates properties that are desirable for a heart-lung system...low weight, small size, high efficiency, high reliability and direct current operability," according to the team.

Other pumps that have been tested for use in heart-lung systems include the roller pump, the single diaphragm pump, the ventricle pump, the impeller pump, the tube compression pump and the cam-driven finger pump. Since the amount of hemolysis is the criterion most often applied to evaluate such pumps, the investigators limited their assessment of the Apollo pump to the degree of resultant hemolysis.

Canine Blood Used

All tests were done at room temperature using fresh canine blood with a hematocrit of more than 35 per cent. Results showed that the average hemolytic index of .0032 for the Apollo pump was over ten times better than the best value for the other pumps, which was 0.04.

"Because it was desired to obtain a baseline evaluation of the ADPP, the pump was not modified in any way nor was it preconditioned with anticoagulant or antihemolysis agents or coatings...Current research is directed toward in vivo testing and variations of the pump frequency, displacement,

and pulsatile signature. Changes in pump materials are being investigated to improve blood compatibility," the investigators stated.

The ADPP is only one aspect of the team's program to develop artificial heart-lung systems. Another is a portable respirator consisting of an oxygen support system for victims of emphysema and chronic bronchitis. Such a portable respirator can improve the quality of life for these persons by allowing them to be ambulatory with adequate oxygen support, the team reported.

Sao Paulo, Rio May Be World's Noisiest Cities

Medical Tribune World Service

RIO DE JANEIRO—Brazil's São Paulo and Rio de Janeiro may be the two noisiest cities in the world, according to the Center for International Environment Information.

Downtown São Paulo averages 105 db at street level, while near Rio beach apartments the level is 85 db. By comparison, mid-Manhattan averages 75 db.

Sound levels double with each 10 db rise.

Retraining Program Set

Medical Tribune Report

PHILADELPHIA—The Medical College of Pennsylvania will hold its ninth retraining program for inactive physicians from May 5 through June 20.